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THE THERAPEUTIC USE OF OXYGEN *

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The use of oxygen in medical therapy occupies at present an uncertain rôle. Previous to the recent war, the current attitude was that of indifference to its use and skepticism concerning its value. This attitude appeared to be based not on inaccurate observation, but for the most part on the true appraisal of results obtained from ineffective methods. The lack of enthusiasm with which oxygen has been regarded in the past seems largely due to the absence of an ideal method of administering it. There is no commonly available method that can supply to the patient an effective concentration of oxygen without in some degree interfering with his comfort. The apparatus most widely used in this country and in England, the tube and funnel, adds less than 2 per cent. oxygen to the inspired air.¹ In short, oxygen was not given in sufficient dosage to get the therapeutic effect. During the war its effective administration in cases of gas poisoning produced such remarkably good results as to offer a stimulus for a renewed investigation of oxygen therapy in clinical disease, as a result of which it is now possible to show that oxygen can be effectively administered with slight or temporary discomfort and with the production of unmistakable improvement in the patient. The purposes of this paper are: (1) through the recent evidence to establish a rational basis for oxygen therapy, (2) to discuss the essential indications for its employment, and (3) to consider briefly the method of administration.

I shall first note the results obtained in the treatment of gas poisoning. When the Haldane apparatus could be used in the acute cases at the front, it was frequently life-saving.² In the treatment of the chronic cases by oxygen chambers in England, remarkable results were obtained by Barcroft³ at Cambridge and by Shufflebotham and Sowry⁴ at Stokes. The gassed soldiers were relieved of palpitation, disordered action of the heart, insomnia, cough, expectoration and mental depression. They showed in many cases a disappearance of polycythemia, and an improvement in their

previously poor cardiac and respiratory responses to effort. These results constitute an instance in which effective treatment with oxygen accomplished definite improvement and cure. Shufflebotham and Sowry treated more than 100 patients in their oxygen chamber, including several patients with pneumonia and pernicious anemia. The pneumonia patients showed an improvement, but in the cases of pernicious anemia a downward progress occurred after they left the chamber.

BASIS FOR RATIONAL USE OF OXYGEN

In discussing the laboratory evidence that forms the basis for the rational use of oxygen, I shall first consider the degree to which anoxemia, or an abnormal lack of oxygen in the body, occurs in clinical disease. The introduction of the arterial puncture by Hürter,⁵ the development of convenient methods of blood gas analysis by Van Slyke⁶ and by Haldane,⁷ and the clinical investigation of Stadie,⁸ Harrop⁹ and Meakins¹⁰ resulted in the establishment of normal standards of oxygen saturation of the arterial blood and in the demonstration quantitatively of the anoxemia present in pneumonia, cardiac insufficiency and emphysema. Means and Newburgh,¹¹ and Lundsgaard¹² had already studied the oxygen of the venous blood. In normal persons the arterial oxygen saturation is about 95 per cent.; in cardiac insufficiency and its complications it may be between 95 and 75 per cent.; in pneumonia, between 95 and 60 per cent. The normal venous saturation is between 65 and 75 per cent.; when a diminished blood flow is present, as in cardiac insufficiency, it may fall between 65 and 30 per cent., depending on the severity of the disturbance.

Since these figures demonstrate that a severe oxygen deprivation may occur in disease, it becomes desirable to know what the effects of such anoxemia are. Fortunately, physiologists have accumulated abundant data on this point. Mountain sickness is a familiar example in which the symptoms are due to oxygen want.¹³ Headache, nausea and vomiting, irrational states, and

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1. Meltzer, S. J.: Therapeutic Value of Oral Rhythmic Insufflation of Oxygen, *J. A. M. A.* **69**: 1150 (Oct. 6) 1917.

2. Douglas, C. G.: Discussion on Therapeutic Uses of Oxygen, *Proc. Roy. Soc. Med. (Sec. Therap. & Pharmacol.)* **13**: 59, 1920.

3. Barcroft, J.; Hunt, G. H., and Dufton, D.: The Treatment of Chronic Cases of Gas Poisoning by Continuous Oxygen Administration in Chambers, *Quart. J. Med.* **13**: 179 (Jan.) 1920.

4. Shufflebotham, F., and Sowry, G. H.: Discussion on Therapeutic Uses of Oxygen, *Proc. Roy. Soc. Med. (Sec. Therap. & Pharmacol.)* **13**: 59, 1920.

5. Hürter: *Deutsch. Arch. f. klin. Med.* **108**: 1, 1912.

6. Van Slyke, D. D.: Gasometric Determination of the Oxygen and Hemoglobin of Blood, *J. Biol. Chem.* **33**: 127 (Jan.) 1918.

7. Haldane, J. S.: New Apparatus for Accurate Blood Gas Analysis, *J. Path. & Bacteriol.* **23**: 443 (Dec.) 1920.

8. Stadie, W. C.: The Oxygen of the Arterial and Venous Blood in Pneumonia and Its Relation to Cyanosis, *J. Exper. Med.* **30**: 215 (Sept.) 1919.

9. Harrop, G. A.: The Oxygen and Carbon Dioxide Content of Arterial and Venous Blood in Normal Individuals and in Patients with Anemia and Heart Disease, *J. Exper. Med.* **30**: 241 (Sept.) 1919.

10. Meakins, J. C.: Observations on the Gases in Human Arterial Blood in Certain Pathological Pulmonary Conditions and Their Treatment with Oxygen, *J. Path. & Bacteriol.* **24**: 87, 1921.

11. Means, J. H., and Newburgh, L. H.: Studies on the Blood Flow by the Method of Krogh and Lindbard, *Tr. A. Am. Phys.*, 1915, p. 51.

12. Lundsgaard, C.: Studies of Oxygen in the Venous Blood, *J. Exper. Med.* **27**: 179 (Feb.) 1918.

13. Haldane, J. S.: Recent Developments in the Therapeutic Use of Oxygen, Contributions to Medical and Biological Research, Dedicated to Sir William Osler **1**: 550, 1919.

mental depression are common symptoms. In carbon monoxid poisoning in which there is often a more abrupt and severe want of oxygen, the patients are usually comatose and have a rapid, feeble pulse, and shallow, rapid respiration. In these patients the anoxemia may have been so severe as to leave permanent damage to the central nervous system. A patient so exposed may in a half hour of vigorous oxygen and carbon dioxid therapy become completely rid of carbon monoxid and have all the hemoglobin fully saturated with oxygen.¹⁴ Nevertheless, he may die one or two days later because of the damage the previous anoxemia created in his central nervous system.¹⁴ This explains why delay in the treatment of a marked anoxemia may result in irreparable injury. In experiments in which a lowered partial pressure of oxygen is breathed in chambers, the results are more easily controlled. Haldane,¹⁵ when exposed to a low pressure of oxygen, became irrational and possessed of a fixed delusion. In summary, it might be said that the disturbance of the gastro-intestinal system is manifested by nausea, vomiting and diarrhea; the respiratory system by increased rate and depth of respiration or by periodic respiration, and later by rapid, shallow respiration; the circulatory system by a constant and progressive increase in pulse rate, and in the end by a fall in diastolic pressure¹⁶ and cardiac failure; the central nervous system by headache, visual disturbances, irrational states and delirium, and finally, coma and death.

A crucial experiment of Barcroft¹⁷ may be cited, since it links up the experimental with the clinical data. He lived for five days in a chamber in which the pressure of oxygen was lowered until his oxygen saturation at rest was 88 per cent. He then experienced the effects of mild anoxemia. His pulse rose from 56 to 86, he was nauseated, racked with headache, and suffered from visual disturbances and vertigo. He became faint on exertion. The arterial saturation of patients with pneumonia frequently falls much lower than that present in Barcroft, thus demonstrating that the ill effects of anoxemia must be an actual accompaniment of clinical disease.

These effects, then, are the result of lack of oxygen, and it is with their prevention or relief by appropriate oxygen treatment that we are now concerned. By application of the methods of gas analysis to blood, and particularly by the successful development of the arterial puncture by Stadie, it was possible to compare the amount of oxygen in the blood before and after treatment with the symptomatic effect. Meakins¹⁸ used the Haldane apparatus in cases of pneumonia, emphysema and bronchitis, and showed that marked improvement in the clinical condition of the patient occurred as the arterial saturation was elevated to the normal. Stadie¹⁹ placed pneumonia patients in a chamber containing between 40 and 60 per cent. of oxygen, and noted that with the removal or decrease in

the arterial anoxemia, a decided improvement in the patient took place. Barach and Woodwell²⁰ used a mouthpiece rebreathing method in the treatment of patients with pneumonia and cardiac insufficiency, and made observations on the oxygen and carbon dioxid contents of both arterial and venous blood. In the cases of pneumonia, the arterial oxygen saturation was either elevated to the normal or much increased. In most of the severe cases, definite clinical improvement could be seen. When edema of the lungs occurred as a complication, the prolonged use of oxygen seemed to avert a fatal outcome.

In cardiac insufficiency, when an arterial anoxemia was present due to passive congestion or edema in the lungs, the inhalation of oxygen raised the arterial saturation to the normal. When acute bronchitis or acute pulmonary edema supervened, the resultant arterial anoxemia could either be entirely removed or much diminished. The improvement in the arterial blood could not always be determined by the degree of cyanosis, as at times progressive heart failure occurred and the stagnant anoxemia masked the improved oxygen saturation of the arterial blood. Obviously, the degree of cyanosis cannot always be used with safety to represent the arterial anoxemia. The venous saturation is needed to give the full picture. Clinical improvement could be seen in the treatment of the acute complications but not in the chronic cardiac condition itself.

The venous saturation in the cases both of pneumonia and of cardiac insufficiency showed an increase that was generally dependent on the increase of the arterial saturation, and merely raised the level at which the oxygen exchange took place. In a few cases there was a slight additional increase that may be explained on the basis of an improved blood flow or on the transfer of physically dissolved oxygen to the hemoglobin as the blood passes from artery to vein. When the patient is breathing a high concentration of oxygen, there may be an excess of oxygen in physical solution amounting to 1 or 2 per cent. by volume, the hemoglobin being fully saturated. As the hemoglobin passes through the capillaries it becomes unsaturated, and it is then possible for the excess oxygen physically dissolved to unite with the hemoglobin and gradually increase its saturation. When the circulation was progressively failing, the venous saturation could not be increased independently of the arterial saturation.

The venous saturation is thus unreliable as a criterion of oxygen therapy, since it varies with the blood flow. It is the oxygen saturation of the arterial blood that is especially significant because it represents the diffusion pressure at which oxygen is available to the tissues. Barcroft²¹ has had calculated the relative amounts of oxygen which would leave the blood to enter the tissues under the three circumstances in which anoxemia exists: (1) the anoxic or arterial; (2) the stagnant or venous, and (3) the anemic. In each case it is assumed that the amount of oxygen going to the tissues in cubic centimeters for each 100 c.c. of blood is the same. In the accompanying table, quoted from Barcroft, it is seen that the arterial anoxemia furnished by far the least oxygen to the tissues, and is thus the most dangerous to the patient.

14. Henderson, Yandell: Personal communication to the author. Haggard, H. W., and Henderson, Yandell: *The Treatment of Carbon Monoxid Poisoning*, J. A. M. A. 77:1065 (Oct. 1) 1921.

15. Haldane, J. S.; Kellas, D. M., and Kennaway, E. L.: *Experiments on Acclimatization to Reduced Atmospheric Pressure*, J. Physiol. 53:181 (Dec.) 1919.

16. Lutz, B. R., and Schneider, E. C.: *Circulatory Responses to Low Oxygen Tension*, Am. J. Physiol. 50:327, 1921.

17. Barcroft, J.; Cook, A.; Hartridge, H.; Parsons, T. R., and Parsons, W.: *Flow of Oxygen Through the Pulmonary Epithelium*, J. Physiol. 53:450 (May) 1920. Barcroft, J.: *Anoxemia*, Lancet 2:485 (Sept. 4) 1920.

18. Meakins, J. C.: *Therapeutic Value of Oxygen in Pulmonary Lesions*, Brit. M. J. 1:324 (March 6) 1920; (Footnote 10).

19. Stadie, W. C.: *The Treatment of Anoxemia in Pneumonia in an Oxygen Chamber*, J. Exper. Med. 35:337 (March) 1922.

20. Barach, A. L., and Woodwell, M. N.: *Studies in Oxygen Therapy. I, In Cardiac Insufficiency and Related Conditions*, Arch. Int. Med. 28:367 (Oct.) 1921; II, *In Pneumonia and Its Complications*, ibid. 28:394 (Oct.) 1921.

21. Barcroft, J.: Footnote 17, second reference.

In summary of the discussion up to this point, it might be stated that the consequences of anoxemia may be serious and harmful, that they exist in clinical disease, and that to a large extent they can be prevented or overcome by appropriate oxygen treatment. It is on this basis that I believe the use of oxygen has a justifiable rôle in medical therapy.

INDICATIONS FOR EMPLOYMENT OF OXYGEN

We come now to the question as to when oxygen should be used. The essential indication for its employment seems to be acute anoxemia. The onset of abrupt want of oxygen indicates prompt treatment to avert the grave effects of severe anoxemia outlined in the beginning of this paper. Chronic anoxemia may, indeed, have ill effects; but its occurrence over long periods of time in patients with congenital or acquired heart disease and in persons who have become acclimatized to high altitudes indicates that no very serious damage is produced.

In the recent Anglo-American expedition to the Andes, all of the party felt poorly when they arrived at the high altitudes, and half of their number were confined to bed with symptoms of acute anoxemia.²² After a time they were able to do their investigative work,

OXYGEN FURNISHED TO THE TISSUES NORMALLY AND IN ANOXEMIA

	Oxygen in Blood Going to Vessels of Tissue Per Cent.	Oxygen Leaving the Blood to Supply the Tissue Per Cent.
Normal*	100	100
Anoxemia:		
Anoxic	66	42
Anemic	66	66
Stagnant	66	75

* The figure 100 at the top of each column is merely a standard with which to compare the figures beneath it.

although more than half of them continued to have symptoms throughout their stay. The natives were also cyanotic, but none had the symptoms of mountain sickness, their condition being that of chronic anoxemia. However, when any one contracted pneumonia, white man or native, it meant practically certain death, unless he could be immediately rushed to the sea level. It is thus apparent that although a chronic anoxemia may be present without symptoms, an acute anoxemia causes definite and perhaps grave injury.

Acute oxygen want occurs in a variety of conditions, among which may be listed pneumonia, acute cardiac failure, severe hemorrhage, epidemic (lethargic) encephalitis, ascent to high altitudes, the complications of chronic cardiac insufficiency, pulmonary edema, acute bronchitis, carbon monoxid poisoning and nitrous oxid and other anesthesia. In acute carbon monoxid poisoning, Yandell Henderson²⁴ found that the symptoms made a swift disappearance when a mixture of oxygen and 5 per cent. carbon dioxide was inhaled. The hyperpnea caused by the carbon dioxide results in a quicker elimination of carbon monoxid and a quicker absorption of oxygen. As in this condition the acute anoxemia may be profoundly dangerous, anything which hastens the return to a normal oxygen content of the blood would appear to be eminently justified. Favorable results from carbon dioxide therapy after anesthesia and operation are also

described by Henderson.²³ The beneficial effects seem to depend on the "augmentation of breathing which rapidly ventilates the anesthetic out of the blood." The circulation is stimulated, increasing the venous return to the heart and raising the arterial pressure. There is, in addition, a marked decrease of post-operative nausea, vomiting and thirst. Five per cent. carbon dioxide has apparently not been harmful when judiciously used. Caution must be exercised, however, in its administration, as larger concentrations may be dangerous. Severe hemorrhage is attended by acute anoxemia of such an extent as sometimes to be the cause of death. Oxygen therapy may in these cases tide the patient over until transfusions can be given.²⁴ In acute cardiac failure and in the acute complications of cardiac insufficiency, the use of oxygen may be of help.

The disease in which acute anoxemia occurs with the greatest frequency and with the greatest severity is pneumonia, and it is here, therefore, that oxygen therapy is most urgently indicated. The use of oxygen can be expected to remove or to diminish the ill effects of acute anoxemia, and in that way to improve the patient's chances of recovery and at times directly avert death. The clinical guide to its use is the presence of cyanosis. In pneumonia, cyanosis has been said to run parallel to the degree of arterial anoxemia.¹⁹ It should be borne in mind, however, that this applies only to patients without anemia. Since the cyanotic color varies with the amount of reduced hemoglobin, a patient with a low hemoglobin may show little or no cyanosis even in the presence of marked arterial anoxemia. As intimated above, the parallelism between the arterial anoxemia and the degree of cyanosis rests on the assumption that stagnant anoxemia is absent. This is generally true as the blood flow in pneumonia, estimated by relative changes in blood gases, appears to be either normal or increased.²⁵ Occasionally a failing circulation does occur with the production of cyanosis of venous rather than arterial origin. It may be stated as a general principle that cyanosis in pneumonia indicates the use of oxygen therapy until it has been removed, or, if that is not possible, until it has been diminished.

The duration and frequency of administration are problems dependent on the individual patient and the resources at hand. It would seem theoretically desirable to keep the patient free from cyanosis as many hours of the twenty-four as possible. In the very severe cases it may be necessary to give oxygen continuously. In the less severe cases benefit may be derived from oxygen administered at frequently repeated intervals.²⁶ The signs which should be kept track of and which usually reflect improvement are: (1) the degree of cyanosis; (2) the pulse rate, and (3) the mental condition of the patient.

23. Henderson, Yandell; Haggard, H. W., and Coburn, R. C.: The Therapeutic Use of Carbon Dioxide After Anesthesia and Operation, *J. A. M. A.* 74: 783 (March 20) 1920.

24. Discussion on Therapeutic Uses of Oxygen, *Proc. Roy. Soc. Med. (Sec. Therap. & Pharmacol.)* 13: 59, 1920. Henderson, Yandell, and Haggard, H. W., with the collaboration of Beatty, H. H.; Brooks, R. W.; Detwiler, S. R.; Ellerbeck, G. C.; Kohle, H.; Robb, H. B., and Taliaferro, W. H.: Hemorrhage as a Form of Asphyxia, *J. A. M. A.* 78: 730 (March 11) 1922.

25. Stadie (Footnote 8). Barach and Woodwell (Footnote 20).

26. Haldane (*Brit. M. J.* 1: 181 [Feb. 10] 1917) has observed: "It may be argued that such measures as the administration of oxygen are at the best only palliative and of no real use, since they do not remove the cause of the pathological condition. As a physiologist, I cannot for a moment agree with this reasoning. The living body is no machine, but an organism constantly tending to maintain or revert to the normal, and the respite offered by such measures as the temporary administration of oxygen is not wasted but utilized for recuperation."

22. Harrop, G. A.: Personal communication to the author.

The degree of cyanosis is, with the exceptions noted above, the most trustworthy clinical guide in the oxygen treatment of pneumonia. Its alteration under treatment may in addition furnish information of prognostic value. Severe arterial anoxemia has been shown to be an unfavorable sign.⁸ If the administration of oxygen fails to remove the anoxemia, or alleviates it only very slightly, the prognosis, in our limited experience, is distinctly worse. Some benefit, however, may be derived from the increase in the oxygen physically dissolved. In cases in which a severe cyanosis is cleared by prompt oxygen therapy, the prognosis is bettered in that the ill effects of anoxemia may diminish or disappear and the patient be thus put in better condition to cope with the specific toxins of the disease.

A careful record of the pulse before, during and after oxygen therapy adds further data on which to judge the effect of treatment. There is usually a distinct slowing in rate. In the severe cases this may be a very striking sign of improvement. In normal persons the inhalation of oxygen causes perceptible slowing of the heart,²⁷ but in patients suffering from anoxemia the decreased rate is usually of much greater extent.²⁰ The reason for this presumably is that anoxemia is itself the cause of rapid heart action. In contrast to the action on the circulation, the respiratory rate is only occasionally slowed and usually is unaffected. What happens to the tidal air in pneumonia as a result of the inhalation of oxygen is still uncertain. In the few observations of Beddard and Pembrey,²⁸ when failure of the right heart occurred, pulmonary ventilation was decreased by oxygen without altering the respiratory rate. In pneumonia unaccompanied by right heart failure or cyanosis, oxygen inhalation for two minutes had little or no effect. It is obvious that more investigation is needed in this field.

An additional effect that may result from the removal of anoxemia is a more alert and a clearer mental condition of the patient. The irrational states and delirium in pneumonia which may in part be due to the anoxemia, as they are producible experimentally by withdrawal of oxygen, do not, however, promptly disappear but seem to follow the clinical course of the disease. It may be that we are dealing here with the effects of long continued oxygen want, which, as intimated above, may persist even after their original cause has been removed.

Subjective dyspnea does not seem to be due to oxygen want, nor is it usually relieved by the inhalation of oxygen. Respiratory distress cannot therefore be taken as a criterion of the therapeutic effect, since as a rule it diminishes only gradually as the general condition improves. Oxygen therapy should be undertaken with the idea that acute anoxemia produces serious and at times grave injury, and not with the idea that the patient will at once be relieved of his respiratory distress and brought to a state of comfort.

The failure to relieve cyanosis represents the infrequent type of response to oxygen therapy. It is presumably due to the existence of a partially intact blood supply through consolidated pulmonary tissue. The fact that the majority of patients are relieved of

arterial anoxemia during the inhalation of oxygen indicates that for the most part pulmonary consolidation is not the precise cause of cyanosis. The presence of edema in or adjacent to the hepatized area or in other parts of the lung appears to be the more important factor. This is more logically related to the ease of removal of anoxemia, since it is highly probable that high pressures of oxygen can diffuse through edema in the bronchioles or through edematous alveoli, whereas, because of the shape of the oxygen dissociation curve, it is hardly conceivable that increased oxygen pressures could make up for an unrespired blood flow through hepatized lung. Pulmonary consolidation, especially lobar, may at times be fairly extensive without the presence of cyanosis, indicating that the blood supply, except for the nutrient bronchial vessels, may be diverted from the area no longer ventilated. Hoover²⁹ found the cyanosis proportionate to the extent of consolidation, and observed that it was relieved by oxygen only when moisture was present in the lungs. Meakins³⁰ found no relation between the degree of anoxemia and the extent of consolidation, and concluded that rapid, shallow breathing was the cause of the anoxemia of lobar pneumonia. We have witnessed extreme shallow respiration result in arterial anoxemia in cases of epidemic encephalitis,³¹ but it has seemed to us only an infrequent factor in the cause of the cyanosis of pneumonia. Pathologic evidence bearing on the question indicates that a certain amount of blood passes through the lung in red hepatization, but none in gray hepatization.³² Cyanosis in pneumonia is thus dependent on the character and stage of the lesion rather than on the actual extent of lung involvement. The major cause appears to be the presence of edema, local or widespread, manifested in the parenchyma of the lung or in the bronchial tree, and susceptible of relief by increased pressures of oxygen. The minor cause is that of an unrespired blood flow through consolidated pulmonary tissue, and is insusceptible of relief by oxygen. Both conditions are more likely to be present in bronchopneumonia, and for that reason cyanosis is here more common and more severe than in lobar pneumonia. An occasional factor that may cause or augment the cyanosis is extreme shallowness of respiration.

We have been concerned with the general effect of the use of oxygen. The injection of oxygen into the peritoneal and pleural cavities or into draining wounds constitutes local individual problems beyond the scope of this paper.

METHOD OF ADMINISTRATION

The method of administration still remains a great problem in oxygen therapy. First of all, it is necessary to provide an effective concentration of oxygen in order to obtain good results. A mixture of air which contains between 40 and 60 per cent. of oxygen seems desirable. Less than 40 per cent. may not be effective, and more than 70 per cent. may be harmful.³³ The exact concentration theoretically required would

29. Hoover, C. F.: Oxygen Therapy, *J. A. M. A.* **71**:880 (Sept. 14) 1918.

30. Meakins, J. C.: Harmful Effects of Shallow Breathing, with Especial Reference to Pneumonia, *Arch. Int. Med.* **25**:1 (Jan.) 1920.

31. Barach, A. L., and Woodwell, M. N.: Studies in Oxygen Therapy, III, In an Extreme Type of Shallow Breathing Occurring in Lethargic Encephalitis, *Arch. Int. Med.* **28**:421 (Oct.) 1921.

32. Gross, L.: Reconstruction of the Circulation of the Liver, Placenta and Lung in Health and Disease, *Canadian M. J.* **9**:632 (July) 1919.

33. Karsner, H. T.: The Pathological Effects of Atmospheres Rich in Oxygen, *J. Exper. Med.* **23**:149 (Feb.) 1916. Flack, M., and Hill, L.: *Textbook of Physiology*, 1919, p. 303.

27. Smith, H. A.: The Effect of Oxygen Inhalation on the Pulse, *Med. Rec.* **1**:481, 1871. Benedict, F. G., and Higgins, H. L.: Effects on Men at Rest of Breathing Oxygen-Rich Gas Mixtures, *Am. J. Physiol.* **28**:1, 1916.

28. Beddard, G. P., and Pembrey, M. S.: Observations on Pulmonary Ventilation in Disease, *Brit. M. J.* **2**:580, 1908.

be that amount precisely needed to remove the anoxemia. Practically, however, there seems to be little need for precision at the present state of our knowledge. The second desirable feature of a good method is that it should produce no discomfort to the patient, or, if that is impossible, slight or temporary discomfort. Thirdly, when prolonged oxygen therapy is planned, the economy of the method has to be considered.

It may be said at the outset that the inhalation of oxygen is the most logical avenue of administration, since it utilizes the vast absorbing surface of the lungs. Other methods, such as the intravenous³⁴ or subcutaneous³⁵ or rectal administration, appear impracticable for prolonged therapy. Exceptions should be made in the case of infants, in whom the subcutaneous use of oxygen has apparently been successfully employed.³⁵

The oxygen chamber is the ideal way to treat anoxemia from the standpoint of effectiveness and comfort, but it is obviously impracticable for widespread use. Modern methods of administration known to us that yield effective oxygen mixtures and that are available for common use are: the Haldane³⁶ apparatus involving the application of the face mask; the Meltzer¹ oral insufflation apparatus, in which a metal tongue depressor is held in the mouth to conduct oxygen; the oxygen tent of Hill,³⁷ which encloses the upper part of the patient in bed; a recent apparatus of Yandell Henderson,³⁸ a description of which has not as yet been published, which also utilizes a face mask, and the mouthpiece rebreathing apparatus which we have used.³⁹ These methods, we believe, all yield an effective concentration of oxygen, but vary in their ability to secure comfort for the patient, and in the economy of operation. It should be added that in infants the nasal catheter may become an effective method because of their small oxygen consumption. The oxygen that enters the lungs through the small catheter contributes in this case a considerable increase of oxygen, whereas in adults it adds relatively so little as to relieve only the rather mild cases of anoxemia. Henderson has added the rubber mouthpiece to his apparatus for patients who will not tolerate the mask. In this method provision is made for the inspiration of a mixture of air and oxygen in the following manner: An amount of oxygen less than the tidal air is run into the collecting bag. During inhalation the oxygen in the bag is exhausted, whereupon an inspiratory valve connected with the outside opens and admits air until the inspired volume is made up. The exhaled air and oxygen are passed out through an expiratory valve. This method would, on the whole, appear to be very satisfactory, although we have not as yet had the opportunity of testing it.

In our apparatus, rebreathing of oxygen was instituted to prevent wastage of the exhaled oxygen, an economy that is to a certain extent offset by the use of soda-lime. The interposition of the rubber tube

between mouthpiece and soda-lime necessitates a little rebreathing of carbon dioxide. If the tube and metal connection are 47 cm. long, with a diameter of 1.2 c.c., the interposed volume is 53 c.c. The tidal air in normal persons is about 500 c.c., and in pneumonia it is rarely below 250 c.c.¹⁹ Rebreathing of carbon dioxide thus occurs to a slight extent and might tend to deepen respirations. It is possible that this action is beneficial in that it decreases the work of the pulmonary bellows by providing a more efficient ventilation. On the other hand, there is some evidence that difficulty in getting rid of carbon dioxide is frequently present in pneumonia.⁴⁰ The dead space would have no action as far as oxygen is concerned, as the entire circuit, including the alveolar air, would be filled with a high concentration of oxygen. The carbon dioxide would not be likely to accumulate to any serious extent since the nose is left open, allowing free diffusion with the outside air. However, it seems on the whole preferable to interpose no additional dead space, and for that reason the apparatus has been modified by the insertion of an inspiratory and expiratory valve and another piece of tubing. The oxygen is thus passed through the soda-lime in a continuous circuit with no rebreathing of carbon dioxide, an idea adapted from the Roth modification of the Benedict portable metabolism apparatus. It is obvious that an expiratory valve could be used in place of the soda-lime, the apparatus then consisting of mouthpiece, expiratory valve, rubber tube and collecting bag. The wastage of the exhaled oxygen would make it a more expensive method, but it would be very simple in operation. It would still possess the advantage of not unduly disturbing the patient, for in our experience the soft rubber mouthpiece caused only slight discomfort, whereas the face mask could rarely be borne because of the marked sense of suffocation it produced.⁴¹

The Meltzer insufflation apparatus requires the constant presence of an attendant to turn the expiratory valve at each expiration and inspiration, and at the same time hold in place the metal tongue depressor that conducts the oxygen. We have had no personal experience with the method, but it does not suggest comfort for the patient, and it would appear a tedious task to operate it over long periods. The oxygen bed-tent represents a more complicated attempt to deal with the problem. In order for it to be successful,

40. Means, J. H., and Barach, A. L.: The Symptomatic Treatment of Pneumonia, *J. A. M. A.* 77: 1217 (Oct. 15) 1921. Barach, A. L.; Means, J. H., and Woodwell, M. N.: The Hydrogen Ion Concentration and Bicarbonate Level of the Blood in Pneumonia, *J. Biol. Chem.* 50: 413 (Feb.) 1922.

41. Since this apparatus has been used by others, several points have come up that are worth mentioning. The rubber mouthpiece as supplied is identical with that used in the Benedict metabolism apparatus. It has a wide margin which fits between the teeth and lips, and prevents leaks in respiration experiments. For oxygen administration, however, the margins should be cut down considerably, as the comfort of administration is greatly increased. One-fourth inch margin opposite the upper and lower lips and one-half inch at the corners is usually satisfactory. At times patients hold the mouth piece more comfortably when the margins are placed behind the teeth rather than between lips and teeth. A water bottle interposed between tank and collecting bag tends to prevent drying of the back of the throat. It is good policy to let the oxygen bubble through the water bottle into the bag continuously rather than to let the bag empty before refilling. This prevents the possibility of nitrogen in the exhaled air unduly accumulating, and insures the breathing of a high concentration of oxygen. The collecting bag does not contain pure oxygen, since the exhaled nitrogen dilutes it slightly. The exact concentration of the mixture, if desired, can be obtained by withdrawing a sample from the attached stopcock and analyzing it in a Haldane or other gas analyzer. It might also be added that coughing does not in any way contraindicate the use of the mouthpiece. It is only the occasional pneumonia patient who coughs frequently during the administration. Under these circumstances he may allow the mouthpiece to slip out by opening his lips and turning his head aside. The metal frame holds the mouthpiece in place so that he may easily close his lips over it when the coughing is over. I have recently added glass mouthpieces with small margins to interchange with the rubber variety when the latter causes salivation. By use of one or the other mouthpiece, a fairly comfortable administration can usually be secured.

34. Tunncliffe, F. W., and Stebbing, G. F.: Intravenous Injection of Oxygen, *Lancet* 2: 321 (Aug. 19) 1916. J. J. A. McMillan: *U. S. Nav. M. Bull.* 13: 88 (Jan.) 1919; 11: 191 (April) 1917.

35. Stuerz, E. Z.: Diätet. in *Physik. Therap.* 7: 67, 159, 1903. Naessens, W. M.: Subcutaneous Injection of Oxygen, *Nederl. Tijdschr. v. Geneesk.* 1: 410 (Jan. 22) 1921. Bayeux, R.: Subcutaneous Injection of Oxygen in Influenza, *Bull. de l'Acad. de méd.*, 1922, p. 176. Howitt, H. O.: Subcutaneous Injection of Oxygen, *Canadian M. A. J.* 4: 983, 1914.

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37. Hill, L.: A Simple Oxygen Bed Tent and Its Use in a Case of Edema and Chronic Ulcer of the Leg, *J. Physiol.* 50, May 24, 1921; *Proc. Physiol. Soc.*, p. 20.

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39. Barach, A. L.: A Simple Apparatus for Administering Oxygen, *J. A. M. A.* 78: 334 (Feb. 4) 1922.

provision must be made to keep it from becoming warm and stuffy, and careful regulation of the contained oxygen and carbon dioxide must be carried out, as in an oxygen chamber, to render it safe. The bed-tent seems to offer great promise for a comfortable and effective method of administering oxygen, although at present it is hardly available for common use.

SUMMARY

The lack of enthusiasm with which oxygen therapy has been regarded seems largely due to the absence of an ideal method of administering it. The successful treatment of gas poisoning by oxygen inhalation during the war offered unmistakable evidence of the favorable results that may follow effective oxygen therapy. This led to a renewed inquiry into the subject of the therapeutic use of oxygen in clinical conditions.

Recent investigation has shown that the effects of acute anoxemia may be harmful, that they exist in clinical disease, and that to a certain extent they can be prevented or overcome by appropriate oxygen treatment. It is on the basis of this evidence that I believe the use of oxygen is a rational and important therapeutic measure.

The essential indication of its employment is acute anoxemia.

Since the abrupt onset of oxygen insufficiency occurs most frequently and most severely in pneumonia, it is in this disease that oxygen therapy is most needed.

33 East Sixty-Eighth Street.

ABSTRACT OF DISCUSSION

DR. WALTER M. BOOTHBY, Rochester, Minn.: It was one of my duties in France to investigate the effect of oxygen treatment in gassed soldiers. I can concur in the advantages obtained from an efficient administration of oxygen as recommended by Haldane in cases of phosgen and chlorine poisoning with edema of the lungs. A thorough clinical trial should be made of oxygen properly administered in an extensive series of pneumonia cases. The apparatus devised by Barach will give oxygen efficiently, and this, or some other apparatus of this type such as that devised by Haldane for use in the army, should be used. Oxygen is not a therapeutic agent in any sense of the word. Its administration merely aids in getting into the body under adverse conditions oxygen in sufficient concentration so that the circulation rate may be decreased. The load on the heart is relieved by increasing the amount of oxygen in the blood through the inhalation of an oxygen percentage from two to three times that contained in ordinary air. Any procedure that will relieve the strain on the heart promises to be of material value in pneumonia.

DR. C. W. GREENE, Columbia, Mo.: I have been much interested in the development of the clinical methods as reported by Dr. Barach and the Rockefeller Institute. In the Air Service the problem is strictly one of oxygen supply. The tests for aviators by the Medical Research Laboratory rest on the reactions a man gives if we gradually shut off the oxygen supply, as in going to the higher altitudes. There are various critical aspects to this question. The answers can be had from experiments with animals and normal men. Such tests determine in no small measure what we may expect from diseased conditions. There are a number of organs and physiologic mechanisms, which Dr. Barach has mentioned, in which lack of oxygen produces a drive to increased work. That undoubtedly involves the respiratory center and the circulation. If the oxygen is progressively reduced, it is surprising how far down the scale one can go without risk. In many persons the reduction of the oxygen in the air breathed can be carried down to 10 per cent. before one can detect any change readily charged to oxygen want. In the human being, "inefficiency" begins somewhere about 8, 7 or 6 per cent. The last thing that is observed is a much

higher respiratory and heart rate. With the higher heart rate, an apparently greater per minute volume of blood is going through the body; hence a faster flow by the absorbing pulmonary tissues and by the peripheral tissues. The point I want to make is that under ordinary conditions, when the oxygen of the air is reduced to 8 per cent. or more, the compensations in the respiratory and circulatory mechanisms take to the tissues all the oxygen they ordinarily use and need. Dr. Carl Greene and I have analyzed venous and arterial blood simultaneously, when the oxygen in the air is reduced to a point at which the animal stops breathing. We have found that the tissues take practically a uniform amount of oxygen until the oxygen of the arterial blood is actually reduced to the level represented by the volume lost in the peripheral tissues. In other words, the tissues get their quota of oxygen if the arterial blood contains about 30 per cent. of the normal amount of oxygen. That means that the percentage of oxygen by volume distributed to the tissues is more adequate in extreme conditions than we have supposed. Now, if the oxygen reduction is below that critical level, then the animal rapidly goes into the condition of extreme decompensation and coma; respiration will stop very soon, though the heart and circulation go on, in an animal, for five or more minutes longer. Experimenters lay less emphasis on the strain of oxygen want on the circulatory apparatus. I think that more stress should be laid on the response of the nervous apparatus. If we put the question another way, it means that if anything occurs to reduce the carrying power of the blood for oxygen, such as the reduction of hemoglobin, there is a far greater physiologic strain than if we reduce the percentage of alveolar oxygen below the normal. It is in the final analysis a question of the volume carrying power of the blood. The increased volume of oxygen inhaled does something in helping to bring matters up to a more nearly normal level, but not so much as many suppose. The percentage of advantage bears no direct ratio to the increased oxygen percentage in the enriched air breathed. The gain to the body, especially the nervous system, by even the fraction of a per cent. of available oxygen working over a long period of time, will sometimes save the day in a losing moment.

DR. R. R. SHIPPEY, Wichita, Kan.: In pneumonia, one of the most vital things is lack of oxygen. The amount of oxygen actually needed may be comparatively small. It seems to me that we have escaped from the old time proposition in treating pneumonia. A few years ago George Douglas Head gave histories of about 1,500 cases treated with free ventilation and cold air, and his death rate was 15 or 20 per cent. Acting on the idea that it was absolutely necessary to make some change because the death rate was so high, he changed his plan almost entirely, and, as far as possible, followed out the plans that our grandmothers used. And his death rate dropped below 3 per cent at once. Years ago, when Willie Jones had "lung fever" and Grandma came in to take care of him he got well. What did she do? Put him in between feather beds, placed a wool sock around his neck, and put goose grease on him. They will recover today if you follow that plan. They will get their oxygen. The congestion in the lungs can be relieved by keeping the surface of the body warm and moist, and they will all recover. In a case of pneumonia, I insist, first, that these patients shall be under blankets. I insist also that they wear some heavy underclothes that cover the shoulders, chest and arms thoroughly. On top of that I want a heavy gown and sweater. How often do we see pneumonia patients in hospitals with head up to the window and only a pink ribbon over the shoulders of the women? They died in a few days.

DR. A. J. CARLSON, Chicago: Has the speaker any statistics proving the value of oxygen in the saving of life or decreasing the symptom in pneumonia? Will the speaker explain how the administration of oxygen in marked lung consolidation can increase the oxygen of the blood? It is very difficult to know what we have done for the pneumonia patient, without very extensive statistics. I am not familiar with any statistics showing that we have actually done anything for a pneumonia patient by letting him breathe 40 or 50 per cent. of oxygen. The mere fact that we are putting 50 per cent. of oxygen into the lungs does not mean that we are increasing the oxygen and decreasing the carbon dioxide in the blood.

DR. HAROLD E. B. PARDEE, New York: Any one who has seen oxygen given to a pneumonia patient would not demand a statistical study of the effect on mortality. It is quite evident that, when a patient who has been cyanotic, dyspneic and with a very rapid pulse shows less cyanosis, less dyspnea and a slowing of the pulse rate after the administration of a certain treatment, this treatment has led to an improvement of his condition, even though it may be a temporary one. This is the sort of change which is produced by proper oxygen administration. The drawback to oxygen administration, as suggested by Dr. Barach, is that it calls for a special device. It is another bit of apparatus for the physician to buy, and because of this it will not be used as much by the physician as the value of proper oxygen therapy warrants. I should like to emphasize that a very good oxygen effect can be obtained by using a tube directly from the oxygen tank, the gas having first bubbled through water so that we can observe its rate of flow, and placing the end of the tube about an inch or an inch and a half from the patient's nostril or mouth, depending on which of these the patient is using for breathing. A stream of oxygen is thus mixed with the inspired air, and I know that this will sometimes produce a beneficial effect, though it probably will not do so as often as a proper rebreathing apparatus. My point is that this is much better than no oxygen at all because of lack of apparatus, and also better than the commonly used funnel method of giving oxygen. Perhaps, after seeing the benefit in a few cases, the physician will feel more ready to own the apparatus. The method is also, of course, wasteful of oxygen.

DR. M. A. MORTENSEN, Battle Creek, Mich.: Four years ago I had the influenza, with a double pneumonia. I remember that as long as I was conscious one of the things I felt I needed was oxygen. Consequently, I offer these suggestions with a great deal of assurance. I was given oxygen by stimulating my heart. Since that experience and reading in the journals of the methods of giving oxygen, and its value, I have used oxygen in a number of cases. And in any case of pneumonia, an extreme case of cardiac inefficiency, especially cases that have developed very suddenly, the administration of oxygen has certainly produced a very apparent change in the patient's condition. There has been a relaxation and better breathing, and a better color is manifested immediately. In a few cases we have obtained definite evidence of the increase of the oxygen content of the blood. Our experience has been that the application has been most agreeable to the patient. The method of application that has been most agreeable has been by putting a tent over the upper part of the bed, a rather small one, and then letting an abundant supply of oxygen from the oxygen tank enter that space. Marked improvement has been evidenced in those cases.

DR. ALVAN L. BARACH, New York: Dr. Greene's work is very interesting. However, his statement that a decrease in the content of oxygen in the arterial blood is of more importance than a decrease in the arterial oxygen saturation is in opposition to the belief expressed by Barcroft, namely, that the arterial or anoxic anoxemia furnishes less oxygen and is more dangerous to the patient than either the anemic or the stagnant type. The fact that an animal may live for a short period of time with an arterial saturation of 30 per cent. hardly justifies one in assuming that serious injury is not taking place. In the chamber and in high altitude experiments quoted in the paper, it is shown that an abrupt lowering of the arterial saturation to 70 or 80 per cent. produces delirious states and other rather well marked symptoms. The factor of the length of time that oxygen want is sustained must be considered. In pneumonia the anoxemia may persist for days and is consequently more serious than a similar deprivation lasting an hour or so. It is interesting that the difference between the arterial and the venous oxygen content remains constant down to an arterial saturation of 30 per cent.; but since we do not know the blood flow, we cannot conclude that the needs of the organism for oxygen are fully satisfied, and certainly we do not know that they are satisfied in a way most advantageous to the organism. In reference to the question of Dr. Carlson as to whether there was any statistical evidence of a reduction in mortality brought about by oxygen therapy: The total number of reported cases of

pneumonia treated effectively with oxygen is as yet too small to present any conclusions purely on the basis of statistics. The clinical improvement in individual cases, with the simultaneous increase in the amount of oxygen in the arterial blood, has been the criterion of its value. The question as to the cause of the cyanosis in pneumonia and the reason that effective oxygen therapy may not invariably relieve it is discussed in the paper. The nasal tube is of help in infants whose oxygen consumption is small. In the mild cases of anoxemia in adults it may also be of help. The bed tent offers great promise, but must be perfected before it can be commonly used.

THE NEW SHORT WAVE LENGTH ROENTGEN-RAY THERAPY*

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Especially within the last three years the interest of the profession in this country has been aroused by claims advanced for the value of the "new deep roentgenotherapy," a method of radiation involving the use of rays of much shorter wave length than have heretofore been available for purposes of treatment. For a decade such physicists as Duane, Des-sauer and Coolidge have been seeking means for producing roentgen rays of wave length nearly approximating the shorter gamma rays of radium. Refinements have been reached in the construction of roentgen-ray apparatus, permitting the maintenance of constant very high voltages (from 200,000 to 280,000) delivered at the roentgen-ray tube terminals. Dr. Coolidge has continued the development of his tube until we now have a type of roentgen-ray tube, capable of withstanding more than 200,000 volts at 8 milliamperes in continuous use. The physical and biologic investigations carried on simultaneously in Europe and America constitute, collectively, one of the most valuable and well-directed pieces of research in the history of medicine, and, for the first time, afford data upon which really precise measurements of dosage in radiation therapy may be based.

It is incumbent on us as surgeons to recognize a certain degree of obligation demanding that we know the essential facts and factors relating to the new method, in order to decide whether or not we are willing to refer our cancer patients to specialists in this penetrating roentgenotherapy. What is the difference between the so-called "new" roentgenotherapy and the type of deep treatment with which we have been more or less acquainted during the last ten or twelve years? Are there dangers inherent in the new method—dangers of damage to skin or deep structures, especially the blood and the blood-forming organs—which suggest reserve? Is it likely, as has been openly charged by some, that the danger of metastasis from malignant lesions is increased? Are the results obtained by the new method notably better than those possible with the equipment and technic already in daily and extensive use? Are there economic considerations which should not be overlooked?

FEATURES OF NEW SHORT WAVE LENGTH ROENTGEN-RAY THERAPY

The following factors are accepted as integral features of the new deep roentgenotherapy:

* From the Surgical Section, Battle Creek Sanitarium.

* Read before the Section on Surgery, General and Abdominal, at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.