Archives of Internal Medicine

VOL. 28

OCTOBER, 1921

No. 4

STUDIES IN OXYGEN THERAPY WITH DETERMINATIONS OF THE BLOOD GASES

I. IN CARDIAC INSUFFICIENCY AND RELATED CONDITIONS *

ALVAN L. BARACH, M.D.

AND

MARGARET N. WOODWELL, A.B.

BOSTON

TABLE OF CONTENTS

1. Harmful effects produced by an insufficient oxygen supply.
2. Evidence that an insufficient oxygen supply exists in clinical disease.
3. Desirability of raising oxygen content of blood to normal level.
4. Methods of administration in recent war.
5. Method developed in this investigation.
6. Illustrative cases of cardiac disease, bronchitis, edema of the lungs. (Pneumonia, edema of the lungs, empyema and respiratory paralysis considered in Papers II and III.)
7. Increase in oxygen content of blood following oxygen inhalation.
8. Clinical improvement that occurs in acute anoxemia, following oxygen inhalation.

INTRODUCTION

The purpose of this investigation was primarily to determine what conditions of oxygen want could be relieved by the therapeutic inhalation of oxygen. The degree of anoxemia was determined by the oxygen saturation of the arterial and venous blood. The effect of oxygen administration was thus quantitatively measured by comparison of values before and after treatment. The correlation of the oxygen changes in the blood with the objective and subjective changes in the patient gave the opportunity of determining whether clinical improvement resulted from oxygen therapy. There were considered in all

* From the Medical Service of the Massachusetts General Hospital. This paper is No. 15 of a series of studies of the physiology and pathology of the blood from the Harvard Medical School and allied hospitals.

* The expense of this work was in part defrayed by a grant from the Proctor Fund of Harvard University for the study of chronic diseases.

two normal subjects, seven patients with cardiac insufficiency, twelve patients with pneumonia, and two patients with lethargic encephalitis. As the cases had to be studied individually, it became advisable for the sake of clearness to divide them into a cardiac group (Paper I), a pneumonia group (Paper II), and a group characterized by a type of shallow breathing in lethargic encephalitis (Paper III). An outcome of the work has been the development of an effective and practicable method of providing oxygen.

HISTORICAL

A few facts will be reviewed from the literature with the purpose of presenting a theoretical basis for the giving of oxygen. Barcroft¹ has shown from his own work and the work of others that any activity of the body organs involves a call for oxygen. Exact measurements have been made for the heart, kidney, muscle and the secreting glands which show that increased work is done only with a proportional increase in oxygen consumption. Stoppage of the oxygen supply brings the perfused heart to a standstill, causes a cessation in the flow of urine, decreases the conduction of nerve tissue, produces muscular fatigue, and at last immobility. Bayliss,² after reviewing the oxygen consumption of resting and active tissues, concluded that "an organ may suffer from oxygen want, even when the venous blood coming from it still contains oxygen, so that the oxygen passes the cells unused. It is probable that for proper functional work, oxygen must be supplied not only in certain amount, but at a tension not far below that in which it is present in the atmosphere and in the arterial blood."

The direct effects of anoxemia, as recently summarized by Haldane,³ have been obtained by observations at high altitudes, by laboratory experiments in which a lowered partial pressure of oxygen is breathed in chambers, and by the consequences of carbon monoxid poisoning, where the oxygen carrying power of hemoglobin is partly destroyed. One of the first symptoms of oxygen want, when gradually produced, is periodic breathing. At high altitudes, this is practically a normal phenomenon. The further symptoms include distinct impairment of mental faculties, often showing itself in manifestations similar to alcoholic intoxication. The powers of judgment, self control, and memory are definitely impaired. After some hours, there are nausea and headache, and often vomiting and diarrhea. If the exposure has been very long, though slight, these symptoms may still persist, even if meanwhile their cause has been removed. When lack of

1. Barcroft, J.: *The Respiratory Function of the Blood*, 1914, p. 105.

2. Bayliss, W. M.: *Principles of General Physiology*, 1918, p. 343.

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

oxygen has been more serious, the pulse becomes rapid and feeble, periodic respiration gives place to rapid, shallow respiration, consciousness becomes greatly impaired or lost, and progressive damage is done to central nervous system, heart and other organs. The evidence is conclusive, Haldane believes, that these characteristic effects are due solely and simply to lack of oxygen.

The existence of cyanosis is *prima facie* evidence of lack of oxygen in clinical disease. Abnormal oxygen unsaturation of the venous blood in cardiac disease was found by Means and Newburgh.⁴ Lunds-gaard⁵ later established the normal values of oxygen saturation of venous blood, and showed in various types of cardiac insufficiency abnormal oxygen unsaturation. The introduction of the arterial puncture by Hürter,⁶ and its successful development by Stadie,⁷ made the arterial blood of human beings accessible for study for the first time. Diminished arterial oxygen saturation was then shown to occur in pneumonia by Stadie,⁷ and in cardiac insufficiency by Harrop.⁸ In these investigations, the close relationship between cyanosis and the amount of reduced hemoglobin in the blood was established. The oxygen saturation of normal resting individuals may be taken as 95 to 98 per cent. for the arterial blood, and 65 to 75 per cent. for the venous blood.

Recently, Barcroft⁹ lived for six days in an atmosphere in which the partial pressure of oxygen fell to 84 mm. On the last day, the oxygen saturation of his arterial blood was 88 per cent., and after the performance of work 83.8 per cent. He lay in the chamber racked with headache, with occasional vomiting, and at times able to see clearly only as an effort of concentration. He became faint on exertion. His pulse, normally 56, had risen to 86. These effects were apparently due purely to oxygen want. The degree of anoxemia that produced them has frequently been found in pneumonia and heart disease by the investigators mentioned above. In many instances, the saturation of the arterial blood falls to far lower levels. It would, therefore, seem likely that lack of oxygen in the degree often found in disease would produce bodily discomfort, disturbances in function and damage to living structure.

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

5. Lunds-gaard, C.: Studies of Oxygen in the Venous Blood, *J. Exper. M.* **27**:179, 1918.

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

7. Stadie, W. C.: The Oxygen of the Arterial and Venous Blood in Pneumonia and Its Relation to Cyanosis, *J. Exper. M.* **30**:215, 1919.

8. Harrop, G. A.: The Oxygen and Carbon Dioxid Content of Arterial and Venous Blood in Normal Individuals and in Patients with Anemia and Heart Disease, *J. Exper. M.* **30**:241, 1919.

9. Barcroft, J.; Cook, A.; Hartridge, H.; Parsons, T. R., and Parsons, W.: Flow of Oxygen Through the Pulmonary Epithelium, *J. Physiol.* **53**:450, 1920.

As a further consideration, there sometimes is an increased metabolic demand for oxygen in the diseases in which anoxemia is itself conspicuous. In cardiac insufficiency, an increased basal metabolism has been demonstrated.¹⁰ Fever causes an increased metabolism which has been proved to be proportional to the increase in fever.¹¹ It is of interest in this connection that the performance of physical exercise in normal men can be done easier, with less dyspnea and less fatigue, when oxygen is added to the inspired air.¹² This has been shown to be especially true of unfit men.¹³ Since oxygen helps the accomplishment of physical work in normal men, it might be expected to aid in the performance of the increased work in cardiac insufficiency and pneumonia. The above favorable results in the absence of anoxemia must depend on the increase of oxygen in physical solution.

We may refer briefly to certain recent methods of giving oxygen. The frequent occurrence of gas poisoning during the war led to a hurried demand for oxygen therapy. The condition produced by the irritant gases was an acute primary edema of the lungs characterized clinically by air-hunger and an extreme degree of cyanosis. Haldane¹⁴ devised an apparatus by which measured quantities of oxygen could be added to the inspired air, thus greatly increasing the available diffusion pressure through the alveolar wall. The essentials were an oxygen tank, a reducing valve, and a face mask. The mask was connected with a collecting bag which received oxygen from the tank, and with the outside air, from which the patient breathed. Oxygen was added to the inspired air in amounts of from one to four liters per minute. This was largely used in the acute cases with generally good results. Douglas¹⁵ found it very effective. Less effective was the nasal tube method, and still less effective and even more wasteful was the tube and funnel method. In the funnel method, Meltzer¹⁶ has calculated that the atmospheric air is not richer by more than 2 per cent., if by so much. Cummins¹⁷ found it difficult to make the

10. Peabody, F. W.; Meyer, A. L., and Du Bois, E. F.: Basal Metabolism of Patients with Cardiac and Renal Disease, *Arch. Int. Med.* **17**:980 (July) 1917.

11. Coleman, W., and Du Bois, E. F.: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, *Arch. Int. Med.* **14**:168, 1914. Also Du Bois, E. F.: Respiration Calorimeter in Clinical Medicine, *Am. J. M. Sc.* **178**:792, 1916.

12. Hill, L., and Flack, M.: Influence of Oxygen on Athletes, *J. Physiol.* **38**:12, 1909.

13. Briggs, H.: Fitness and Breathing, *J. Physiol.* **54**:292, 1920.

14. Haldane, J. S.: Therapeutic Administration of Oxygen, *Brit. M. J.* **1**:181, 1917.

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

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

17. Cummins: Discussion on Therapeutic Uses of Oxygen, *Proc. Roy. Soc. Med. (Sec. Therap. & Pharmacol.)* **13**:59, 1920.

men stand the mask of the Haldane apparatus. Ryle¹⁸ used the nasal catheter, introduced by Stokes, with fairly good results. Masks were improvised at his station, but were not tolerated by the men. Hamil¹⁹ considered the nasal tube satisfactory, but wasteful, and also found the mask badly tolerated, especially in warm climates. Hoover²⁰ said the gassed men begged to be relieved of the mask and preferred to have the oxygen conducted by a soft rubber tube in their nostrils, though by the latter method he did not see a single case in which the cyanosis was diminished.

The chronic cases of gas poisoning were treated in oxygen chambers at home, with striking evidences of improvement. The group described by Barcroft, Hunt and Dufton²¹ exhibited disorder action of the heart, nocturnal dyspnea, high red blood cell counts, low percentages of carbon dioxid in the alveolar air, acidosis and kindred conditions. The patients were kept in a chamber of 50 per cent. oxygen for sixteen out of the twenty-four hours for five days. Almost all of them showed a disappearance of symptoms. Shufflebotham and Lowry²² treated cases of chronic gas poisoning in oxygen chambers with equally marked improvement. They also treated one case of lobar pneumonia and one case of bronchopneumonia with promising results. Meakins²³ treated a case of chronic gas poisoning with the Haldane apparatus, giving oxygen for three one-hour periods daily for seven days. The patient became cured of all symptoms. The arterial oxygen saturation was normal at the beginning, and increased by oxygen. He also reported three cases of pneumonia and five cases of asthma, emphysema and chronic bronchitis, in which the arterial saturation was elevated by oxygen administration, and in whom marked improvement resulted. No determinations of the venous blood were done, nor were any cases of cardiac insufficiency studied. For patients who will not, or cannot, put up with a mask, Hill²⁴ constructed a simple oxygen bed tent, which encloses the upper part of the patient when in bed. Arrangements are made for inlet and outlet of air and oxygen, for absorption

18. Ryle: *Ibid.*

19. Hamil: *Ibid.*

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

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

22. Shufflebotham, F., and Lowry, G. H.: *Discussion on Therapeutic Uses of Oxygen*, Proc. Roy. Soc. Med. **13**:59, 1920.

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

24. 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.

of carbon dioxid, and for circulation of the air. A window of non-inflammable celluloid is placed in front of the patient. A soldier was treated who had had his femoral artery tied, and suffered from coldness, blueness, edema and chronic ulcers of the leg. In forty-eight hours, the oxygen made the extremity warm and of good color, removed the edema, cleaned up the ulcers, and started the healing in a remarkable way.

METHODS

The methods used in this investigation for giving oxygen have represented a gradual development in the apparatus used and in the duration of treatment. With the purpose first of determining to what extent and for what length of time oxygen could be increased in the blood, short periods of administration were given. Later, prolonged and repeated administration of oxygen was given with more of a therapeutic object. The first apparatus consisted simply of a face mask, connected through a soda-lime canister with a rebreathing bag, in turn connected with an oxygen tank. In this way, the patient rebreathed pure oxygen, the carbon dioxid being absorbed by soda-lime. This was soon modified by the insertion in the mask of a small inlet and outlet valve connected with the outside air. This provided the patient with about an 80 per cent. oxygen mixture. All the connections were made one inch wide so that no resistance was felt on respiration. This was efficient, easily put together, and economical in the expenditure of oxygen. Its disadvantage was the use of the mask. There were a few patients who took it without objection and in comparative comfort. The greater number could not bear the suffocating feeling which they said it produced, and struggled against it. Especially when the patient was suffering with urgent dyspnea, or in warm weather, the mask was poorly tolerated. Later, when the Haldane apparatus was used, the same difficulty was experienced. When the patient was in coma the Haldane apparatus was very useful, for it was convenient to adjust the inlet of oxygen to the rate desired and leave it on for long periods. For the patients who would not submit to oxygen administration by a mask of any sort, a soft rubber mouthpiece such as is used in the Benedict Respiration apparatus was tried in its place with the rest of the rebreathing outfit unchanged. This proved to be very satisfactory. It fits easily into the mouth, its opening is wide enough for all respiration to take place through it, and its flanged margins support it and prevent leaking. When held or attached so that no pressure is brought to bear on the patient's mouth, it is comfortable, and causes nothing in the way of suffocation. When the nose is held, pure oxygen is rebreathed. This diminishes comfort, and was found to be unnecessary and undesirable, since patients get a rich oxygen mixture even when breathing through nose and mouth. The patient is asked

to breathe through his mouth, and usually adapts himself easily to the mouthpiece, breathing from four to seven parts oxygen through his mouth, and from three to six parts air through his nose. In the pneumonia patient, breathing takes place through mouth and nose even more naturally, and a mixture of about 50 per cent. oxygen is usually inhaled. By watching the excursion of the rebreathing bag, the percentage of oxygen being breathed can be roughly estimated. The nose is held closed for a few inspirations, making all respiration take place through the mouth. When the nose is released, the diminution in the excursion of the bag indicates the proportion of breathing through the nose. This is, of course, only approximate, but there is no need for knowing the precise composition of the mixture. (Where this is desired, a Douglas bag can previously be filled with a known mixture of oxygen, and attached in place of the tank.) There seem to be two important considerations in giving oxygen: one, that an effective oxygen mixture be used; two, that pure oxygen should not be given for long periods. Lorrain Smith²⁵ was able to produce pneumonia in animals by having them live in atmospheres of pure oxygen for several days. Karsner²⁶ also produced pneumonia in rabbits by having them breathe from 80 to 90 per cent. oxygen in chambers for two or more days, but was able to demonstrate no noteworthy changes in other organs. Mixtures under 70 per cent. oxygen can be breathed indefinitely without harmful effect.²⁷ That no increase in the vital process occurs during the inhalation of pure oxygen was first demonstrated by Lavoisier and Seguin²⁸ in 1789, and after a century of dispute was finally carefully confirmed by Benedict and Higgins.²⁹

There are patients who will for a while inhale through the mouth and exhale through the nose or inhale through the nose and exhale through the mouth, in the first case not rebreathing and consequently wasting the oxygen, and in the second place distending the rebreathing bag. This is usually remedied by instruction. There are, of course, patients in active delirium who will not put up with mask or mouthpiece. As a rule, however, the patient takes the mouthpiece well, and breathes a satisfactory mixture. No matter how ill, it involves no actual burden; patients who struggled against the mask frequently took the mouthpiece quietly and even dozed off during the administration. (See illustration for arrangement of apparatus).

25. Smith, J. L.: The Pathological Effects Due to Increase of Oxygen Tension in the Air Breathed, *J. Physiol.* **24**:19, 1899.

26. Karsner, H. T.: The Pathological Effects of Atmospheres Rich in Oxygen, *J. Exper. M.* **23**:149, 1916.

27. Flack, M., and Hill, L.: *Textbook of Physiology*, 1919, p. 303.

28. Lavoisier and Seguin: *Mem. de l'Acad. des Sc.*, 1789, p. 185.

29. Benedict, F. G., and Higgins, H. L.: Effects on Men at rest of Breathing Oxygen-Rich Gas Mixtures, *Am. J. Physiol.* **28**:1, 1916.

The apparatus is easily put together and carried about, and is not wasteful in its consumption of oxygen. (The duration and efficiency of the soda-lime can be tested by running the air in the rebreathing bag through a barium hydrate solution.)

The gas analysis, except for the instances mentioned below, was done by Van Slyke and Stadie's³⁰ method of determining oxygen and carbon dioxide on the same sample of blood. A modified Van Slyke vacuum apparatus is used, in which the pipet is twice the length and one-half the diameter of the original one, and calibrated to 0.01 c.c. The Van Slyke³¹ method of determining oxygen alone (with the recent correc-

Apparatus for giving oxygen. The patient breathes through the rubber mouthpiece M through the can of soda-lime C into a rebreathing bag B. The carbon dioxide exhaled is removed by the soda-lime, and oxygen is admitted from the tank O at a sufficient rate to keep B inflated. In this way the patient rebreathes pure oxygen from the apparatus, but since his nose is left open he dilutes this with a certain proportion of atmospheric air. In practice this results in the inhalation of from 40 to 60 per cent. oxygen.

tions for dissolved gases) was used in Case 4, the analyses in Case 3 that were done Oct. 16 and Oct. 20, 1921, and the analyses in Case 2 that were done Oct. 6, 1921. The arterial and venous blood was drawn without stasis under oil after the method described by Stadie.⁷ The analyses were done in duplicate, in most cases directly after the blood was taken. When the blood was allowed to stand from one to three

30. Van Slyke, D. D., and Stadie, W. C.: J. Biol. Chem., To be published.

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

hours it was kept on ice. Lundsgaard found that blood under oil on ice suffered no change in oxygen content in twenty-four hours. Control determinations done by ourselves at these varying intervals showed no significant change in gas content.

PRESENTATION OF DATA

It will help in the consideration of our cases if the several types of anoxemia are borne in mind. According to the classification of Barcroft,³² they are as follows:

1. *Anoxic Type*.—The pressure of the arterial blood is too low. The arterial oxygen saturation of the hemoglobin is below normal, i. e., below 95 per cent. Mountain sickness is an example in which the diminished partial pressure of oxygen in the blood is due to the diminished partial pressure of oxygen in the atmosphere. In edema of the lungs, the oxygen at prevailing pressures cannot diffuse properly through the diseased alveolar wall, and some unrespired blood is passed into the aortic stream, lowering the arterial saturation.

2. *Stagnant Type*.—The quantity of oxygen which reaches the tissues in unit of time is less than normal because of a slowed blood flow. More oxygen is used up in the capillaries and the venous blood has a lowered oxygen saturation, below 65 per cent.

3. *Anemic Type*.—A diminished amount of available hemoglobin is present, which involves a lessened capacity to carry oxygen. This condition may be due to an actual diminution in the number of red blood cells, or the hemoglobin may be converted into methemoglobin, or monopolized by carbon monoxid so that its oxygen carrying function is destroyed.

The anoxic type is primarily due to pulmonary causes, i. e., faulty oxygenation of blood as it flows through the lungs. The stagnant type is primarily due to cardiac causes, i. e., decreased rate of blood through the systemic capillaries. In cardiac insufficiency, the two frequently occur together, the stagnant type because of poor heart action, the anoxic type because of the secondary conditions of pulmonary congestion and edema.

PROTOCOL OF EXPERIMENTS

The individual cases follow, the first two being normal controls:

CASE 1 (Table 1).—Normal. White female, research worker; age, 23 years.

EXPERIMENT.—Nov. 18, 1920. Subject in recumbent position, three hours after breakfast. Pure oxygen was given through a mask for one-half hour. There was no change in color of skin or mucous membranes. No change subjectively. Venous saturation before oxygen 67.7 per cent.; after, 69.1 per

32. Barcroft, J.: Anoxemia. *Lancet* 1:487, 1920.

cent.; venous carbon dioxid content before, 51.3 volume per cent.; after, 53 volume per cent. Pulse: 66 before, 60 after. Respiratory rate: 14 before, 16 after. Blood pressure: 140/80 before, 135/85 after. Vital capacity: 3,564 c.c. before, 3,424 c.c. after. Electrocardiogram showed normal rhythm before, and no change during or after oxygen.

CASE 2 (Table 1).—Normal. White male, physician; age, 26 years.

EXPERIMENT.—Oct. 6, 1920. Subject in recumbent position, forty-five minutes after lunch. Pure oxygen administered through a mask for one-half hour. Arterial saturation before, 96.6 per cent.; after, 99.6 per cent.; venous saturation 71.3 per cent. before. Venous blood at end of administration was taken after wrist had been bandaged tightly at site of artery puncture, and hence blood was under stasis when drawn. The saturation even under these conditions was 72.8 per cent.

EXPERIMENT 2.—Dec. 15, 1920. Subject in recumbent position, four and one-half hours after breakfast. Pure oxygen given through mask for one-half hour. Pulse before, 76; after, 68. Respiration before, 19; after, 21. There seemed to be deeper breathing during oxygen. Venous oxygen saturation: 73.5 per cent. before, 83 per cent. after. Venous carbon dioxid content: 52.4 volume per cent. before, 50.2 volume per cent. after.

In a normal man, the inhalation of oxygen for one-half hour increased definitely the oxygen content and saturation of arterial and venous blood. In a second individual, the inhalation of oxygen for the same period increased the oxygen content and saturation of venous blood to a very slight extent. The carbon dioxid content of venous blood was not markedly or consistently altered, although slight changes occurred in each experiment. These may have been produced by a change in breathing incident to the mask. Subjectively, there were no effects. Objectively, the slowing of the pulse was the only other definite finding. The blood pressure, vital capacity, rate of respiration, and electrocardiogram showed no significant changes.

REPORT OF CASES

CASE 3 (Table 2).—T. M., white, male, coachman; age, 57 years.

Diagnosis.—Cardiac insufficiency, chronic myocarditis, partial heart block, right bundle branch block.

History.—Rheumatic fever when young, without cardiac symptoms. Ten years alcoholic history. Fifteen months before this admission, patient first noticed dyspnea and swelling of the legs. Since then he has never been well, and, for the six weeks before entry he has suffered from dyspnea, orthopnea and swelling of the legs and abdomen.

Physical Examination.—Oct. 15, 1920. Orthopnea and periodic respiration. Slight cyanosis of lips and mucous membranes. Moderate distention of neck veins. Heart much enlarged, apex in sixth space in anterior axillary line. Sounds regular, rapid, of poor quality. Systolic murmur over entire precordium. Pulse full, rate 90. Artery wall thickened. Blood pressure, 158/105. Dulness, diminished breath sounds, and moist râles at both bases. Shifting dulness in abdomen. Marked edema of legs. Irrational most of the time. Temperature normal. Urine: Specific gravity, from 1.022 to 1.030; slight trace of albumin. Blood Wassermann negative. Enlarged heart with widened arch on roentgenogram. Electrocardiogram showed delayed conduction and right bundle branch block. Nonprotein nitrogen 45.6 mg. per 100 c.c.

Course and Treatment.—Confined to bed; fluids restricted to 1,500 c.c.; digipuratim, 6 grains daily from Nov. 15 to 20, 1920.

On the night of admission, 400 c.c. of blood was removed, with a little relief.

Oct. 16, 1920: Condition same as on admission. At 10 a. m., oxygen saturation of the arterial blood was 87.5 per cent.,³³ the venous saturation 53.2 per cent. At 2:30 p. m., the venous saturation was 41.6 per cent. The only change was that he was more irrational in the afternoon. Pure oxygen was given through a mask uninterruptedly for one-half hour. At the end, the arterial saturation was 99.5 per cent., the venous saturation, 68.4 per cent. Fifteen minutes after the administration, the venous saturation was 67.4 per cent. The patient took the mask without complaint, and said he felt more comfortable after the inhalation. Periodic respiration was present before oxygen. After four minutes breathing became regular, of moderate depth, rate 30 per minute. One minute after removal of mask periodic respiration recurred. Cyanosis of lips disappeared and the ears became pink during the inhalation. Pulse: 90 before, 84 immediately after, 84 fifteen minutes after oxygen.

October 17: No cyanosis evident. Periodic respiration. Pulse 60.

October 19: Slight cyanosis of lips. Periodic respiration. Pulse 64.

October 20: Face a grayish dusky color, lips slightly cyanotic. Periodic respiration with long periods of apnea. Distention of neck veins, congestion in lungs, and edema of extremities were undiminished. Pulse from 40 to 50. Digitalis was stopped, 30 grains of digipuratim having been administered since admission. Oxygen was given through a mask for one-half hour. Arterial saturation before oxygen 83.5 per cent.; one and one-half hours after, 89.9 per cent. Venous saturation before, 53.7 per cent.; at the end of fifteen minutes oxygen, 71.6 per cent.; at the end of thirty minutes oxygen, 72.4 per cent.; one and one-half hours after the inhalation, 72.4 per cent. During the administration, his face noticeably pinkened, and dilated capillaries and venules stood out a bright red. After one minute's oxygen, the periodic respiration was changed to regular breathing, rate 32, finally slowing to 25. Five minutes after the administration, it was still regular, rate 26. Fifteen minutes later, Cheyne-Stokes respiration had recurred, with, however, short periods of apnea, in contrast to the long apneic periods present before oxygen. The pulse exhibited striking variations. At the start it was regular, rate 48 (digitalis effect). During the inhalation it became very irregular, rate rising to 88, until the end of the administration, when it again became regular, rate 68. Five minutes later, it was 48 and regular.

October 21: Patient was much quieter, more comfortable and slept better. Cheyne-Stokes respiration continued most of the time with short periods of apnea, rate 26. No cyanosis. Dilated venules and capillaries on face remained pink. Pulse from 50 to 60. Venous saturation 78.1 per cent. Venous carbon dioxid content 61.4 volume per cent.

October 23: No cyanosis, but face was pale. Signs of congestion in lungs less marked. Edema of legs a little diminished.

October 25: General condition unchanged. Cheyne-Stokes breathing present. Arterial saturation 96.6 per cent., venous saturation 77.4 per cent. Arterial carbon dioxid content, 56.2 volume per cent.; venous carbon dioxid content, 61 volume per cent. Oxygen was given for one-half hour, a valve effect in the mask being utilized to provide about 70 or 80 per cent. mixture. The mask was first connected with the room air. In one minute, periodic respiration was replaced by regular breathing, rate 33. Air was breathed for six minutes, and respiration continued regular, rate from 33 to 36 per minute.

33. The attempt was made to draw the arterial blood equally during apnea and dyspnea, but this could only be crudely approximated. That the phases of periodic respiration make an important difference in oxygen content is shown by subsequent determinations.

Oxygen was then given, and the breathing continued at about the same rate. His color previous to oxygen was pale, without cyanosis. After oxygen, his nose, cheeks, lips and ears were pink, and the dilated capillaries and venules became prominent and red. The pulse again showed interesting variations. Prior to the giving of oxygen, the rate varied with the phase of respiration, in dyspnea 48 per minute, in apnea 84 per minute. (Duration of apnea fifteen seconds.) During the inhalation the pulse rate quickened, and became very irregular, the irregularity being felt at the wrist as dropped beats, rate 88. Five minutes after oxygen, the pulse rate was 73, without dropped beats but varying slightly with the Cheyne-Stokes respiration, which had returned at this time. Shorter periods of apnea, however, were present, and the pulse variations were likewise smaller than before oxygen. At the end of the administration, the patient was asked to lie flat to see whether orthopnea persisted in the presence of a plentiful oxygen supply. He complained of immediate discomfort, and was allowed up. Patient was not clear mentally, and this response may have been a habit sensation rather than actual discomfort. The arterial saturation, taken forty minutes after the treatment, was 97.7 per cent., the arterial carbon dioxid content 59.2 volume per cent. The vital capacity immediately before oxygen was 1,194 c.c.; immediately after, 1,166 c.c.; two hours later, 1,166 c.c.

October 29: Clinical condition little changed. For past four days he has been allowed up in chair part of the day in attempt to restore clear mentality. Vital capacity 1,530 c.c.

October 31: Got up at night, walked about, fought efforts to replace him.

November 1: Temperature 101.5 F. Patient developed an acute bronchitis. Face had a dull grayish appearance; there was moderate cyanosis of lips and chin, and slight cyanosis of ears. Frequent productive cough present. He was more irrational. Cheyne-Stokes respiration continued. Pulse 100 in apnea; 80 in dyspnea. Vital capacity 942 c.c. Lungs showed scattered sibilant and sonorous râles over both chests, with dulness, diminished breathing and moist râles at right base. Mask was connected to room air to test effect on breathing. No change occurred, Cheyne-Stokes breathing persisting for entire fifteen minutes of experiment. An attempt was made to get arterial blood separately in apnea and dyspnea but the syringe filled too slowly to get unmixed samples. The arterial saturation obtained in apnea was 85.2 per cent., in dyspnea 87 per cent.; the arterial carbon dioxid content in apnea was 56.7 volume per cent., in dyspnea 59.3 volume per cent.

November 3: Temperature fell to 99.5 F. Periodic respiration present with periods of apnea lasting from 15 to 20 seconds. Samples of arterial blood were obtained with less overlapping today. The arterial saturation in apnea was 78.3 per cent., in dyspnea 85.2 per cent. The arterial carbon dioxid content in apnea was 61.4 volume per cent., in dyspnea 62 volume per cent. Oxygen was given through a mask for one-half hour. At the start, the mask was connected with the room air, and in one minute the respiration became regular. When the mask was removed, Cheyne-Stokes breathing immediately recurred. The mask was then adjusted connected with oxygen, and in one minute the breathing again became regular, rate 34. At the end of the administration the cyanosis had completely disappeared. The capillaries and dilated venules on the face stood out bright red. The venous saturation was 94.5 per cent. The arterial saturation was not tested, but was obviously raised to the normal or above. Before oxygen the pulse was 96 in apnea and 56 in dyspnea. The electrocardiogram showed auriculoventricular block and right bundle branch block; in the dyspneic phase, sino-auricular slowing and increase of auriculoventricular block; in the apneic phase, increase of sino-auricular rate without dropped beats. During oxygen administration, with regular breathing, the pulse was regular, rate 84 to 92. The electrocardiogram confirmed the regularity, showed an absence of the marked auriculoventricular block, a decrease in the height of the R wave and less notching of the R complex.

Ten minutes after the administration periodic respiration began again, though with much shorter periods of apnea. Pulse 88 in apnea, 74 in dyspnea. The electrocardiogram preserved the characteristics it had during oxygen administration. One-half hour later, pulse and electrocardiographic findings were the same. Two hours later, pulse and respiratory variations were the same as after oxygen. Immediately after oxygen, patient noticed no subjective relief; two hours later he said he breathed more easily. No cyanosis was evident. Blood pressure before and after inhalation 150/110. Vital capacity before, 942 c.c.; after, 858 c.c.

November 4: No cyanosis evident. On the following morning he was removed to a chronic cardiac convalescent hospital. He died Nov. 8, 1920.

In this case, a diminished oxygen saturation was present in both arterial and venous blood. The arterial (anoxic) anoxemia may be accounted for by the edema and passive congestion at the bases of the lungs, the venous (stagnant) anoxemia by the insufficient circulation. Oxygen inhalation raised the saturation of the arterial and venous blood to the normal level. The elevation of the arterial oxygen content naturally causes a corresponding elevation of the venous content, the respiratory exchange taking place at a higher level. In addition to this relative increase of venous oxygen, there was an additional increase that seems best explainable on the basis of an improved blood flow. The relative permanency of the elevated venous saturation tested at frequent intervals over a period of several days is further evidence that the circulation was improved by the increased supply of oxygen. The objective changes were in a measure confirmatory. The cyanosis disappeared for several days at a time. The pulse when regular was slowed. When the heart was under the influence of digitalis or of the phases of periodic respiration, the changes were more complicated. The periodic respiration was temporarily changed to regular respiration by the inhalation of oxygen. However, in two out of three trials, the mere application of the mask connected with room air was sufficient to cause regular respiration. No significant change in blood pressure, vital capacity, urinary secretion, or carbon dioxide content of arterial and venous blood resulted from oxygen inhalation in the amount given. The electrocardiographic changes indicate a lesser degree of block during during and following the administration of oxygen. Subjectively, he usually said that his breathing was better or that he felt more comfortable, but he was never enthusiastic. It seemed that the mask contributed somewhat to lessening his sense of relief, as it was often hot and wet with perspiration at the end of the administration.

CASE 4 (Table 2).—G. W., colored, male, fireman; age, 57 years.

Diagnosis.—Cardiac insufficiency, syphilitic aortitis, aortic regurgitation, right hydrothorax.

History.—Rheumatism at 7, chancre at 23. In good health up to four years ago, when dyspnea, palpitation of heart and cough first occurred. During the months before admission he suffered from increasing dyspnea and orthopnea, massive edema of extremities and progressive distention of abdomen.

Physical Examination.—Oct. 4, 1920. Periodic respiration alternated with frank dyspnea. No cyanosis of mucous membranes. Heart much enlarged, downward and to the left. Blowing diastolic murmur over aortic area, and systolic murmur at apex; rate, 88. Corrigan and capillary pulse. Blood pressure, 190/60. Dulness and moist râles at bases of lungs, with diminution of breath sounds on right. Massive edema of extremities. Abdomen distended, no free fluid. Liver not felt. Urine showed a trace of albumin, specific gravity from 1.019 to 1.030. Phenolsulphonephthalein excretion 45 per cent. in two hours. Nonprotein nitrogen, 30 mg. per 100 c.c. Blood Wassermann strongly positive.

Course and Treatment.—Confined to bed; restricted fluids; digipuratum from October 6 to 8, in all 8 grains; evening sedative of morphin or veronal.

October 7: Patient in hospital three days with no change in physical signs, or any improvement in comfort. Oxygen was given through a mask attached to rebreathing apparatus for one-half hour. Oxygen saturation of arterial blood before administration, 87.6 per cent.; after, 99 per cent. Venous saturation before, 71 per cent.; after, 78.5 per cent. Pulse 84 before, 82 after. Respiration 34 before, 40 after. Objectively there were no other changes. Immediately after administration, he said he felt about the same. In the evening he felt distinctly better and thought the oxygen had helped him. Sleep was better that night than previously.

October 8: Decided diuresis occurred. Urinary output increased from 360 to 960 c.c., with an intake less than usual, 480 c.c., instead of the average daily intake of 800 c.c. Digipuratum had been given on three previous days, 8 grains in all.

October 10: Patient slightly irrational. Marked bradycardia and vomiting resulted from digitalis. Pulse, though regular, had been brought from 88 to 48. He was very uncomfortable. Oxygen was given through mask for one-half hour. Venous saturation before, 57.3 per cent.; at the end of fifteen minutes, 86 per cent.; at the end of thirty minutes, 91.4 per cent. Periodic respiration was replaced after one minute's oxygen by regular rapid respiration, rate 40 per minute. Pulse remained low, between 45 and 50. Subjective response was that he felt a little sleepy at the end of the administration. No diuresis followed.

October 22: His course has been apparently stationary. He showed at this time most of the evidences of cardiac insufficiency that he did on admission, including persistence of lung signs. The oxygen saturation of the arterial blood was 89.9 per cent., the venous saturation 69.4 per cent. He was removed to his home on the following day. He died there one month later.

In this case of decompensated syphilitic heart disease, the arterial (anoxic) anoxemia was fully corrected by the inhalation of oxygen. The venous saturation, within normal limits after three days' rest in bed, was increased by oxygen inhalation. The marked slowing of the heart due to digitalis was attended with a fall in venous saturation, apparently to the degree of a stagnant anoxemia, and suggests that the use of digitalis in regular hearts to the point of marked slowing causes a diminution in circulatory efficiency.

CASE 5 (Table 2).—M. T., white, male, tailor; age, 68 years.

Diagnosis.—Cardiac insufficiency; chronic myocarditis; auricular fibrillation; auriculoventricular block; right bundle branch block; emphysema; chronic bronchitis; polyserositis.

History.—No rheumatic or venereal history. For many years previous to 1911, he took two glasses of brandy daily. During the past thirteen years he

has suffered from cough and dyspnea, which have gradually but progressively become worse, until now he is practically bedridden. Cyanosis has been evident for five years. His abdomen has been tapped repeatedly for four years, at first every three months, now every three weeks. He lives at home, coming to the hospital only for paracentesis.

Physical Examination.—Eight years ago he had an enlarged, regular heart without evidence of valvular disease, enlarged liver and spleen, emphysema and chronic bronchitis. His heart is now of huge size, extending into the mid-axilla. Electrocardiographic tracings have shown progressive changes, first a lengthening of the P-R interval, then right bundle branch block (slight alteration in the arteriogram, and finally auricular fibrillation. The other conditions also advanced, but to a less degree. The cyanosis was the most striking feature of the case, and he was called "the blue man."

Nov. 9, 1920: At rest on a couch, he was moderately dyspneic. Ears, cheeks and nose were a reddish blue, lips a dark, deep blue, hands a bluish bronze color. The tips and borders of his tongue were purple. He was able to lie flat for two and one-half minutes, after which he became very uncomfortable. Lying flat was attended with an even greater degree of cyanosis. Oxygen was given through a mask for two five-minute periods, but he complained that it suffocated him. The rubber mouthpiece was then tried (for the first time) and he breathed through it readily. This was given for twenty minutes, the nostrils held occluded most of the time. The ears and nail-beds of the fingers pinkened slightly. The cheeks and hands were still markedly cyanotic, though less so than previously. The lips were still darkly cyanotic. The venous oxygen saturation before the administration was 29.6 per cent., twenty minutes after it was 82.4 per cent. Venous carbon dioxid content was 58.4 volume per cent. before, 47.4 volume per cent. twenty minutes after. Pulse (no deficit) from 50 to 64 before; from 54 to 66 after. Respiration, from 24 to 26 before, 28 after. Blood pressure, 115/55 before; 112/56, after. Vital capacity of the lungs 1,026 c.c. and 1,222 c.c. before; 1,110 c.c. after. Urine acid before, alkaline one-half hour later. Electrocardiogram showed auricular fibrillation and right bundle branch block. After oxygen, the notching of the R wave was less marked, and the height of the R wave was lowered. After the inhalation the patient (without any questioning) expressed decided increase in his general comfort and in his breathing.

November 18: Patient was seen in his home. He had an acute exacerbation of his chronic bronchitis. Respiration was accompanied by much wheezing. Sibilant and sonorous râles heard throughout both chests. Cyanosis very marked. Abdomen was more distended with fluid. Oxygen was given through the mouthpiece. A Douglas bag had been previously filled with a 60 per cent. oxygen mixture, and left at the bedside in place of an oxygen tank. A two-way valve was inserted in the circuit, and patient gave oxygen to himself, twice a day for forty-five minutes at a time. This was repeated on the following day.

November 20: Cyanosis noticeably diminished by oxygen of two previous days. Dyspnea was still present, and abdomen was accumulating more fluid. Oxygen was again given as before, except that a 75 per cent. oxygen mixture was supplied. Breathing was again described by the patient as "easier" after oxygen. Cyanosis was strikingly diminished in hands and ears, and finger nails were slightly pink. Lips were still blue, though less so than previously. Arterial oxygen saturation before today's inhalation was 86.3 per cent.; one hour after, 95.6 per cent. Venous saturation, 46.4 per cent. before; two days later, 57.8 per cent. The arterial carbon dioxid content was 47.7 volume per cent. before, 49.9 volume per cent. one hour later. The venous carbon dioxid content was 53.2 volume per cent. before, and 53 volume per cent. two days later. Pulse 60 before treatment, 48 one hour later; respiration 22 before, 23 one hour later.

November 22: No oxygen given for two days. Acute bronchitis largely dissipated. Color like that one hour after oxygen two days ago. Abdomen distended with fluid and respiration was difficult. Arterial saturation 97.8 per cent., venous saturation 57.8 per cent. Arterial carbon dioxide content 52.6 volume per cent.; venous carbon dioxide content, 53 volume per cent. Pulse 50, respiration 24.

November 24: Patient seen after paracentesis. Felt much relieved. Breathing better after removal of fluid. Fingers and hands showed only slight cyanosis. He said his hands had not been so free from cyanosis for years and reiterated that the oxygen treatment at his home made him much more comfortable and improved his breathing.

Patient was not treated further with oxygen. He continues to come to outpatient clinic for paracentesis.

This case is an example of chronic arterial (anoxic) and venous (stagnant) anoxemia, the former element being due to emphysema, chronic bronchitis, and passive congestion at the bases of the lungs, and the latter to a slowed, insufficient blood flow. It is a striking illustration of the fact that a severe lack of oxygen, even of anoxic type, may last for years without disastrous effects, if it supervenes very gradually. The saturation of the arterial and venous blood was raised to the normal by the administration of oxygen. The venous saturation in auricular fibrillation changes from minute to minute depending on the output from the heart, but the change in these experiments was too great to be accounted for in this way. The difference in color of the blood before and after oxygen, from an almost black to a bright red, was more striking in this case than in any of the others studied. A certain amount of permanency in the raised oxygen content of the blood and in the clinical improvement occurred. The electrocardiographic changes again involving intraventricular block may, perhaps, indicate a lesser degree of block during oxygen administration. It is interesting that the cyanosis was only little altered after the first single administration of oxygen, but became definitely relieved after continued administration, although in each case the blood values showed great improvement.

CASE 6 (Table 2).—L. J., white, male, cabinet maker; age, 62 years.

Diagnosis.—Myocardial insufficiency; auricular fibrillation; cardiac hypertrophy.

History.—No rheumatic, tonsillar, or venereal history. Ten years ago, first suffered from dyspnea on exertion, palpitation and precordial pain. Never had edema of extremities. Three subsequent attacks occurred. Present break in compensation is similar to previous ones.

Physical Examination.—March 21, 1921. Face deeply flushed. Lips red, with cyanotic overcast. Finger nails, cheeks and ears slightly cyanotic. No dyspnea at rest. Heart markedly enlarged, completely irregular, without murmurs. Blood pressure, 170/100. Moist râles at both bases; diminished breath sounds at right base, and bronchovesicular breathing at left back below angle of scapula. Liver edge palpable 5 cm. below costal margin. Urine: specific gravity, from 1.014 to 1.020; very slight trace of albumin. Blood

Wassermann negative. Nonprotein nitrogen, 41.4 mg. per 100 c.c. Phenol-sulphonephthalein excretion, 35 per cent. in two hours. Red blood cell count, 6,100,900. Hemoglobin, 154 per cent. (oxygen capacity). Vital capacity, 1,754 c.c.

Course and Treatment.—Confined to bed, salt-free low protein diet; convallaria, 5 c.c., three times a day, March 25 and 26 (used in a separate investigation).

March 25, 1921: Condition unchanged. Vital capacity 1,866 c.c. Oxygen given through mouthpiece for one-half hour. Oxygen saturation of the arterial blood before the inhalation, 86 per cent.; after, 98.1 per cent.; venous saturation before, 53.4 per cent.; after, 47.8 per cent. Arterial carbon dioxide content before, 40.3 volume per cent.; after, 41.3 volume per cent.; venous carbon dioxide content before, 48.2 volume per cent.; after 49.9 volume per cent. The cyanosis gradually cleared, leaving the lips deep red, and giving an increased pinkness to rest of face. No change of a consistent nature occurred in cardiac, pulse, or respiratory rate. Electrocardiographic tracings showed auricular fibrillation unchanged, before and after. The patient said he felt better after the inhalation. He breathed about 80 per cent. oxygen. The cyanosis began to return directly after the administration, and in half an hour was again marked, not seemingly to the degree before oxygen. On the following day, no effect of the oxygen inhalation could be seen clinically. Vital capacity, 1,474 c.c.

March 29: Condition unchanged. No dyspnea at rest. Cyanosis was not definitely altered. Arterial oxygen saturation 88.3 per cent.; venous saturation, 58 per cent. Arterial carbon dioxide content, 42.7 volume per cent. Oxygen was given through a mouthpiece for one hour, patient breathing about 50 per cent. oxygen. Clinical effects were similar to previous administration. Blood not tested. Vital capacity before oxygen, 1,726 c.c.; day after oxygen, 1,838 c.c.

Patient left the hospital two weeks later. Seemed to have less dyspnea on exertion. Cyanosis was still present, a little less marked. Signs in lungs largely persisted.

The exact diagnosis of this patient remained in doubt. The signs in the lungs were those of passive congestion, and apparent compression of the left lower lobe from the large heart. The anoxemia was both arterial (anoxic) and venous (stagnant), and of marked degree in proportion to the other symptoms. The chronic nature of the diminished oxygen content of the blood was manifested by the polycythemia. Inhalation of oxygen completely relieved the arterial anoxemia, though only temporarily. The lowered venous content of oxygen can be explained by the varying output from the heart occurring in auricular fibrillation. Lundsgaard⁵ showed that the venous oxygen content in auricular fibrillation may be normal in the stage of decompensation, and also that it might be abnormally lowered in full compensation. It is obvious that the venous saturation cannot be used as a criterion of oxygen therapy when the auricles are fibrillating.

CASE 7 (Table 2).—S. M., white, housewife; age, 68 years.

Diagnosis (necropsy).—Cardiac insufficiency; cardiac hypertrophy and dilatation; pulmonary edema; pulmonary thrombus.

History.—Shortness of breath and fatigue for two years. Two months before entry, patient began to suffer from a sense of suffocation, and pronounced dyspnea and orthopnea. Swelling of legs and ankles, continued nausea, and general weakness caused her to enter the hospital.

Physical Examination.—Oct. 25, 1920: Dyspneic and orthopneic. Slight cyanosis of mucous membranes. Lungs, anteriorly and posteriorly, filled with fine and medium moist râles. Heart much enlarged, downward and to left. Sounds muffled, regular, without murmurs. Blood pressure, 190/110. Pulse full and bounding; rate 78; no thickening of radial artery. Veins of neck extremely distended. Fluid wave and shifting dullness in abdomen. Massive leg edema. Phenolsulphonephthalein excretion 30 per cent. in two hours. Non-protein nitrogen 40 mg. per 100 c.c. of blood. Urine, specific gravity, from 1.020 to 1.022; trace of albumin; occasional cast. White blood cells, 17,000; polymorphonuclears, 90 per cent. Blood Wassermann, negative.

Course and Treatment.—Confined to bed; fluids restricted to 800 c.c.; digipuratum, October 25 to 28, in all 20 grains.

Oct. 27, 1920: Condition unchanged. Patient was very restless and anxious. Arterial saturation, 90.7 per cent.; venous saturation, 69 per cent. Arterial carbon dioxid content, 39 volume per cent.; venous carbon dioxid content, 45.2 volume per cent.

October 28: Dyspnea continued. Face was of a grayish dusky color, with moderate cyanosis of the lips. Râles in lungs were of coarse moist variety. Arterial saturation, 88 per cent.; venous saturation, 74.5 per cent. Arterial carbon dioxid content, 43.5 volume per cent.; venous carbon dioxid content, 46.5 volume per cent. Oxygen was given through a mask connected with a Douglas bag containing a 60 per cent. oxygen mixture. Three fifteen-minute periods were given, separated by five-minute intervals. Patient took the mask poorly, and it was stopped because of the discomfort it gave her. One-half hour later, the arterial saturation was 90.9 per cent.; the arterial carbon dioxid content, 43 volume per cent. No improvement in color, respiration, pulse or distention of neck veins was observed. On questioning, she said she breathed easier after the oxygen. She was then given pure oxygen for three five-minute periods, after which the administration was finally stopped because of patient's discomfort in breathing through a mask. Pulse 90 before oxygen, 104 after. Respiration 27 before, 36 after. Vital capacity, 672 c.c., before; 450 c.c. after. Blood pressure, 205/118 before; 210/120 after. There seemed to be the very slightest alleviation of the cyanosis of the lips as a result of the oxygen. No further administration was attempted. She became increasingly cyanotic, and died at five the next morning.

At necropsy a large hypertrophied and dilated heart was found, without evidence of valvular disease. There was sclerosis of the aorta, pulmonary and renal arteries. In branches of the right pulmonary artery leading to the inferior lobe of the right lung, grayish-red thrombus masses were seen, with corresponding areas of lung infarction. The lung tissue of both lungs was moist, leathery, and of a salmon pink color. The trachea and bronchi were bathed in muco-pus.

The anoxemia in this case was of the anoxic type, arising obviously from the congestion and edema of the lungs. This was not successfully overcome by oxygen in the period given, although it was partially relieved. The mask was so disturbing to the patient as to render its use impossible, and accounts for the elevation in pulse and respiration. (The mouthpiece had not been thought of at the time this patient was studied.)

CASE 8 (Table 2).—J. V., white, housewife; age, 50 years.

Diagnosis.—Cardiac insufficiency, rheumatic mitral valvular disease; chronic myocarditis; auricular fibrillation; pulmonary edema. (At necropsy, deformity of the mitral, tricuspid and aortic valves, elevated fibrous plaque at beginning of right coronary artery were found.)

History.—Tonsillitis, followed by rheumatism, when 23 years old. For past sixteen years patient has had dyspnea on exertion. Nine days ago, was abruptly seized with palpitation of heart and dyspnea, followed the day after by substernal pain, vomiting, sleeplessness and weakness.

Physical Examination.—Oct. 19, 1920: Marked dyspnea and orthopnea. No cyanosis. Heart greatly enlarged, completely irregular, with systolic and diastolic murmurs at apex and at aortic area. Apex rate, 140; pulse rate, 128. Blood pressure, 120/85. Lungs clear. Liver not palpable. Slight edema over tibia. Urine: specific gravity, from 1.026 to 1.028; slight trace of albumin. Blood Wassermann, negative. Phenolsulphonaphthalein excretion, 20 per cent. in two hours. Nonprotein nitrogen 60 mg. per 100 c.c. Electrocardiogram showed auricular fibrillation, left ventricular preponderance.

Course and Treatment.—Confined to bed; soft solids; digifolin 4 c.c., and dipuratum 9 grains, from Oct. 19 to 26, 1920; evening, sedatives of morphin.

Oct. 26, 1921: Course in hospital showed no improvement. On the previous night, restlessness and insomnia being unrelieved, hyoscin hydrobromid, 0.01 grain, was given. In the morning she was in coma, and outspoken edema of the lungs was present. Frothy mucus filled the mouth and throat. Face was a dusky gray; lips, hands and finger nails were deeply cyanotic. Respiration was moderately deep, rate 37. Pulse was scarcely palpable, completely irregular, and very rapid. Veins were collapsed. Oxygen saturation of the arterial blood was 76.1 per cent. Arterial carbon dioxide, 39.2 volume per cent. Because of agonal condition of patient, oxygen administration was not delayed to get venous saturation. Pure oxygen was given through a mask for two hours and twenty minutes. At the end of forty minutes the venous saturation was 43.8 per cent., taken while she was breathing oxygen. The venous carbon dioxide content was 52.2 volume per cent. No change clinically could be observed. At the end of one hour, the pulse became temporarily palpable, but quickly tapered off into a thready run which could not be counted. At the end of two hours, it became palpable for several minutes. At this time the lips showed a distinct diminution of cyanosis, and there was less cyanosis in the fingers and hands. No change in breathing was observed, and frothy mucus continued to collect in the back of the throat. Arterial oxygen saturation was 97.7 per cent.; the arterial carbon dioxide content, 45.7 volume percent. At the end of two hours and twenty minutes the venous saturation was 59 per cent., the venous carbon dioxide content 55.2 volume per cent. The administration was then stopped. Face, lips, hands, finger nails, and upper portion of chest speedily became a deep blue, and she died twenty minutes later.

In this case, a severe arterial (anoxic) anoxemia was caused by widespread edema of the lungs; the venous (stagnant) anoxemia was caused by acute heart failure. Cyanosis showed no distinct relief until oxygen had been given for two hours. Arterial saturation at that time showed that the oxygen content of the arterial blood had been raised to the normal. The long time that was required to alleviate the cyanosis was a surprising feature. The abundance of foam and mucus in the bronchial tree and the existence of a venous anoxemia are probably accountable for this, since the former delayed the passage of the oxygen and the latter masked the improvement. The elevation of the venous saturation is probably largely explained by the raising of the arterial saturation. The carbon dioxide content of arterial and venous

blood steadily rose, indicating that the edema fluid hindered the respiratory exchange in the lungs. An acidosis was probably present, due to carbon dioxid accumulation.

CASE 9 (Table 2).—H. R., colored, male, janitor; age, 45.

Diagnosis.—Cardiac insufficiency; chronic myocarditis; asthma; chronic bronchitis; pulmonary edema.

History.—No rheumatic or syphilitic history. One pint of whisky daily for many years. Shortness of breath and cough began three years ago. During the past six weeks cough, dyspnea and discomfort have been extreme, and extremities became swollen.

Physical Examination.—Feb. 3, 1921: Marked dyspnea, respirations rapid and shallow; rate 45; moderate cyanosis of mucous membranes. Lungs full of sibilant, sonorous and medium-sized moist râles, more in front than back. Heart much enlarged. Sounds regular, rapid, poor quality. No murmurs. Blood pressure, 145/105. Vessel wall palpable. Liver dullness extends to umbilicus in right midclavicular line. Moderate leg edema. Urine: specific gravity, from 1.012 to 1.020; albumin, slight trace. Phenolsulphonaphthalein excretion, 50 per cent. in two hours. Nonprotein nitrogen, 74.1 mg. per 100 c.c. Blood Wassermann, negative.

Course and Treatment.—Confined to bed; fluids restricted to 1,500 c.c.; digitalis leaves, 2 grains, three times a day; evening sedatives. Patient's course was stationary for seven days, and then took a sudden change for the worse.

Feb. 10, 1921: He was found comatose in the early morning. Respirations rapid and shallow, rate 45. Lips and mucous membranes quite cyanotic. Pupils pin-point, and react very slightly to light. Pulse 128, small, easily compressible. Heart sounds not heard because of gurgling noises during respiration. Lower half of anterior chest is filled with medium and coarse moist râles, posteriorly moist râles are scattered throughout.

Oxygen was administered through the Haldane mask, at the rate of four liters per minute for fifteen minutes. No change in condition was observed, and rebreathing apparatus was substituted, with valve attachment to the mask affording about 80 per cent. oxygen. One-half hour later patient was bled 500 c.c. Oxygen was kept up for three hours. Pulse had gradually fallen to 100; respirations varied between 36 and 44; cyanosis had disappeared. Patient at times moved about in bed, opened his eyes, and showed signs of returning consciousness. After oxygen had been administered for forty-five minutes the arterial blood showed a saturation of 100 per cent.; the venous saturation was 53.6 per cent. Arterial carbon dioxid content was 75.0 volume per cent.; venous carbon dioxid content, 82.4 volume per cent. The pulse rate remained down the rest of the day, and there was no cyanosis.

February 11: Patient looked much better in the morning. He was still dyspneic, but cyanosis was absent. He seemed rational and answered questions. Moisture in lungs continued. In the afternoon he swiftly became very cyanotic, dyspneic, and finally comatose. The oxygen saturation of his venous blood was 0.3 per cent.; the carbon dioxid content, 63.4 volume per cent. Oxygen was administered as on the previous day. Cyanosis was much diminished, though still present. Pulse slowed from 112 to 100. Oxygen was stopped after two hours, and patient died one hour later.

Asthma, bronchitis, and edema of the bases of the lungs were responsible for the arterial (anoxic) anoxemia. The development of general pulmonary edema introduced a very grave state of oxygen want. The inhalation of oxygen plus venesection tided him over for one day. On the following day, a sudden recurrence of anoxemia,

largely due to cardiac failure and shown strikingly in the venous saturation, was only partially relieved by oxygen. Death occurred one hour after oxygen was stopped, due apparently to cardiac failure.

DISCUSSION

It is interesting to note that all of the patients had an arterial (anoxic) anoxemia, which we must attribute to the associated pulmonary conditions. Most of them had a stagnant type of anoxemia, which can be attributed directly to the insufficient output from the heart. The cases, it may be observed, were selected usually because of the presence of cyanosis and do not represent all varieties of cardiac insufficiency, since in some cyanosis is entirely absent.

These cases showed uniformly an increase in the oxygen saturation of the arterial blood following short periods of oxygen inhalation. When passive congestion and edema were localized at the bases, or in the presence of acute bronchitis or chronic bronchitis and emphysema, the relief of arterial (anoxic) anoxemia was comparatively prompt. When widespread edema of the lungs was present, more prolonged administration of oxygen was required to elevate the arterial saturation.

The mechanism of elevation of the arterial saturation seems to depend on the increased diffusion pressure of oxygen available in oxygen-rich mixtures. In the cases in which passive congestion and edema are confined to the bases, the arterial anoxemia arises presumably because the swelling and edema in the alveolar wall act as a hindrance to the normal diffusion of oxygen.

In widespread edema of the lungs, the fluid in the alveoli and bronchial tree inhibits the free passage of air. In acute bronchitis, excess moisture in the bronchi and bronchioles acts in a similar way. These hindrances to the normal exchange of oxygen are apparently overcome by an increased diffusion pressure of oxygen. A second factor to be considered in the elevation of the arterial saturation is the shallow character of the pulmonary ventilation and the related diminution of the vital capacity of the lungs that occurs in cardiac insufficiency. Shallow breathing, although brought about by anoxemia, is itself a cause of anoxemia.³⁴ That this plays any great rôle in the production of the anoxemia of heart disease or in its alleviation is at present in doubt. In this series, no significant changes in rate of respiration occurred, except in the change from periodic to regular breathing. Beddard and Pembrey³⁵ found a decrease in pulmonary ventilation

34. Haldane, J. S.; Meakins, J. C., and Priestley, J. G.: The Effects of Shallow Breathing, *J. Physiol.* **52**:449, 1919.

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

during oxygen inhalation in four cases of cardiac failure, without change in rate. If this is a constant occurrence, oxygen inhalation does nothing in the way of removing shallow breathing, but merely increases its effectiveness. According to Haldane, Meakins and Priestley,³⁴ however, shallow breathing may arise in heart disease with impaired circulation as a direct result of the anoxemia. In their experiments on normal individuals it was found that shallow breathing caused uneven ventilation of the lungs, which in turn caused anoxemia, periodic respiration and other symptoms. These effects were made worse when the subject assumed the recumbent position, and this was made the basis of the explanation of orthopnea in cardiac insufficiency. They state that "since the orthopnea is due to shallow breathing caused by and intensifying anoxemia, it is clear that the condition can be treated by adding oxygen to the air inspired." In the cases of our series, it frequently seemed that the breathing was deeper during oxygen inhalation, but since no exact measurements were made no conclusions can be drawn, and it remains for further investigation to determine the precise rôle of shallow breathing in heart disease. It is our impression that it may augment a previously existing arterial anoxemia, but that it is not ordinarily of the extent to be the primary cause.

Periodic respiration has been considered a manifestation of slight degrees of oxygen want. In these cases, it was constantly changed to regular breathing by oxygen administration. However, immediately after the mask was removed, with the blood still normally saturated with oxygen, the periodic respiration usually recurred. Further, it was sometimes changed to regular respiration by the application of the mask connected with the room air. Although oxygen deficiency is probably its essential cause, there are other factors such as the patient's attention and habit, which operate in its continuance.

Cardiac dyspnea in the cases studied seemed to have little relation to the degree of anoxemia, either anoxic or stagnant. Further, the inhalation of oxygen, although it completely relieved the anoxemia, produced only slight or moderate relief of the dyspnea. In accordance with these facts, we hold the belief, expressed by previous investigators, that lack of oxygen is not the important cause of cardiac dyspnea, even in the presence of marked cyanosis. It seems rather to be regarded as an important and dangerous byproduct. The carbon dioxid contents of the arterial and venous blood in three cases showed a decrease in alkali reserve, and in two cases an apparent increase. As a result of oxygen therapy, there was frequently a slight increase in carbon dioxid content. In a recent study of the carbon dioxid dissocia-

tion curve in cardiac decompensation, Peters³⁶ expresses the belief that the cause of the dyspnea is the fact that a greater ventilation is necessary to effect the normal carbon dioxid elimination, with the additional factors in some cases of a carbon dioxid acidosis (with actual lowering of the p_H), and in others a reduction of the available alkali of the blood. In four tested cases, an increase in the normal difference between the arterial and alveolar carbon dioxid tension was found. That an inefficient pulmonary mechanism for the exchange of the blood carbon dioxid is at the basis of cardiac dyspnea is indeed strongly suggested by Peters' work. That a mechanical factor, the diminution of the vital capacity emphasized by Peabody,³⁷ is the important cause of the inefficient pulmonary ventilation involves, it seems to us, a necessary addition to the theory of cardiac dyspnea.

The venous saturation was regularly increased by oxygen inhalation except in one case of auricular fibrillation. In this condition, the varying output from the heart results in a variable venous saturation, which, therefore, becomes an unreliable criterion for oxygen therapy, just as it is of circulation efficiency. The elevation of the venous saturation in the main represented and was due to the elevation in arterial saturation, the respiratory exchange taking place on a higher level. In addition to this relative increase of venous oxygen, there was in three cases a further increase that seems best explained on the basis of an improved blood flow. In two cases tested at frequent intervals, the elevated venous saturation had a certain degree of permanency, which again suggested that the circulation was bettered by the increased supply of oxygen. The relief of the cyanosis and the slowing of the pulse were in a measure confirmatory.

It must be recognized that a venous saturation below 65 per cent. does not indicate that the circulation is impaired, unless the arterial saturation is normal. In order to determine whether there is circulatory defect, the difference between the arterial and venous saturation must be obtained and compared with the normal difference. If it is increased, an inefficient circulation is indicated. This difference has been emphasized by Means and Newburgh⁴ as the significant determination in the estimation of blood flow from oxygen values, and was first discussed by Krogh and Lindhard³⁸ and termed by them the coefficient of utilization of the oxygen carrying power. The normal

36. Peters, J. P., and Barr, D. P.: The Carbon Dioxid Dissociation Curve and the Carbon Dioxid Tension of the Blood in Cardiac Dyspnea, *J. Biol. Chem.* **45**:559, 1921.

37. Peabody, F. W., and Wentworth, J. A.: The Vital Capacity of the Lungs and Its Relation to Dyspnea, *Arch. Int. Med.* **20**:443, 1917.

38. Krogh, A., and Lindhard, J.: Measurements of the Blood Flow Through the Lungs of Man, *Skand. Arch. f. Physiol.* **27**:100, 1912.

range is between 20 and 30 per cent., since the normal arterial saturation is about 95 per cent. and the venous saturation between 65 and 75 per cent. The determination of cardiac insufficiency on the basis of the oxygen unsaturation in volume per cent. or the oxygen consumption in volume per cent., introduces a factor which has little relation to blood flow, namely, hemoglobin. The upper limit of normal for these values has been placed by Lundsgaard⁵ and Harrop⁸ at 8 volume per cent. Now, if a patient's hemoglobin registers 43 per cent. according to the Haldane scale, his oxygen capacity is only 8 volume per cent. In order for him to show any cardiac insufficiency on this standard the oxygen unsaturation would have to be over 8 volume per cent., which is manifestly impossible as he does not possess

TABLE 1.—EFFECT OF OXYGEN ON THE BLOOD GASES IN TWO NORMAL INDIVIDUALS *

Case No.	Diagnosis	Date, 1920	Oxygen Inhalation	Oxygen Content		Oxygen Saturation		Oxygen Capacity Vol. %	Hemoglobin Calculated from Oxygen Capacity	Carbon Dioxide Content	
				Arterial Vol. %	Venous Vol. %	Arterial %	Venous %			Arterial Vol. %	Venous Vol. %
1	Normal	11/18	Before oxygen		11.52		67.7	17.03	92.1		51.3
			Oxygen for 30 min.		11.78		69.1	(17.03)	(92.1)		53.0
2	Normal	10/ 6	Before oxygen	16.79	12.88	96.6	71.3	17.38	94.0		
			Oxygen for 30 min.	17.30	12.64	99.6	72.8†	(17.38)	94.0		
	Normal	12/15	Before oxygen		14.63		73.5	19.92	107.9		52.4
			Oxygen for 30 min.		16.51		83.0	(19.92)	(107.9)		50.2

* Subject in recumbent position.

† At end of oxygen administration wrist was tightly bandaged at site of artery puncture, and hence venous blood in this instance was under stasis when drawn.

the available hemoglobin. For an estimation of blood flow, then, the venous unsaturation in volume per cent. would be accurate only to individuals with a normal hemoglobin, whereas the venous saturation in per cent. and the coefficient of utilization would hold good for all patients since it gives the relative usage of the hemoglobin.

The slowing of the pulse that occurred in the normal individuals occurred to a greater extent in the presence of anoxemia. Slowing of the heart in normal men was first observed by Smith³⁹ and recently carefully confirmed by Benedict and Higgins.²⁹ The blood pressure and vital capacity showed no immediate relation to oxygen deficiency or its correction. The electrocardiogram in the normal and in a case of uncomplicated auricular fibrillation showed no alteration. In two

39. Smith. H. A.: The Effect of Oxygen Inhalation on the Pulse, Med. Rec. 1:481, 1871.

TABLE 2.—EFFECT OF OXYGEN INHALATION ON THE BLOOD GASES IN SEVEN CASES OF CARDIAC INSUFFICIENCY

Case No.	Diagnosis	Date	Oxygen Inhalation*	Oxygen Content		Oxygen Saturation		Oxygen Capacity, Vol. %	Hemo-globin Calcu-lated from Oxygen Con-tent	Carbon Dioxid Content		Remarks
				Arte-rial Vol. %	Ve-nous Vol. %	Arte-rial %	Ve-nous %			Arte-rial Vol. %	Ve-nous Vol. %	
3	Cardiac insufficiency; chronic myocarditis; partial heart block; right bundle branch block	10/16/20	4 hrs. before oxygen...	16.52	10.05	87.5	53.2	18.90	102.1	...	...	Periodic respiration
			Before oxygen...	...	8.16	...	41.6	19.62	106.1	...	...	...
			Oxygen for 30 min.	19.51	13.41	90.5	68.4	(19.62)	(106.1)	...	...	Regular respiration
		10/20/20	15 min. after oxygen...	...	13.21	...	67.4	(19.62)	(106.1)	...	...	...
			Before oxygen...	18.29	11.73	83.5	53.7	21.88	118.9	...	...	Periodic respiration
			Oxygen for 15 min.	...	15.69	...	71.6	(21.88)	(118.9)	...	...	Regular respiration
		10/21/20	Oxygen for 30 min.	...	15.81	...	72.4	(21.88)	(118.9)	...	...	Periodic respiration
			1½ hrs. after oxygen...	19.68	13.81	89.9	72.4	(21.88)	(118.9)	...	...	Periodic respiration
			24 hrs. after oxygen...	...	15.91	...	78.1	20.40	110.3	...	...	Periodic respiration
		10/22/20	Before oxygen...	18.97	12.55	...	68.1	19.00	109.8	...	...	Periodic respiration
4	Cardiac insufficiency; syphilitic aortitis; aortic regurgitation; right hydrothorax	10/23/20	Before oxygen...	17.94	14.02	96.6	77.4	18.90	102.1	56.2	61.0	Periodic respiration
			40 min. after oxygen...	15.44	12.72	97.7	79.7	18.39	99.4	59.2	59.7	Periodic respiration
			No oxygen — apnea	13.78	15.44	85.2	...	18.12	96.0	56.7	56.7	Acute bronchitis developed
		11/ 1/20	dyspnea...	...	9.73	...	...	...	...	59.3	...	Cyanosis +++
			No oxygen...	15.70	...	87.0	...	(18.12)	(98.0)	...	...	...
			Before oxygen—apnea	17.14	...	78.3	53.6	(20.17)	(108.9)	61.4	65.1	Cyanosis +++
		11/ 3/20	dyspnea...	...	...	85.2	...	(20.17)	(108.9)	62.0	...	Cyanosis 0
			Oxygen for 30 min.	...	19.03	...	94.5	(20.17)	(108.9)	...	...	After 3 days in bed
			Before oxygen...	13.70	12.72	97.6	78.5	(17.90)	97.1	...	...	Excess of digitalis
		10/ 7/20	Oxygen for 30 min.	17.71	14.04	99.0	87.3	20.31	109.8	...	...	...
5	Cardiac insufficiency; chronic myocarditis; aortic regurgitation; right bundle branch block; Myocardia infarction; pulmonary embolism	10/10/20	Before oxygen...	...	11.02	...	57.3	(20.31)	(109.8)	...	...	...
			Oxygen for 15 min.	...	17.45	...	86.0	(20.31)	(109.8)	...	...	...
			Oxygen for 30 min.	14.16	18.33	...	91.4	(20.31)	(109.8)	...	...	...
		10/22/20	No oxygen...	...	10.91	...	69.4	15.77	86.2	...	...	...
			Before oxygen...	...	6.32	...	29.6	21.32	115.1	...	58.4	Oxygen for one-half hour
			20 min. after oxygen...	...	17.58	...	82.4	(21.32)	(115.1)	...	53.2	Oxygen given on 2 previous days
		11/ 9/20	Before oxygen...	18.24	9.83	...	...	21.18	114.2	...	...	...
			Before oxygen...	18.64	...	96.6	...	19.50	105.2	49.9	...	...
			1 hr. after oxygen...	...	10.90	...	57.8	18.89	102.0	52.6	53.0	...
		11/22/20	48 hrs. after oxygen...	18.64	9.83	...	...	19.50	105.2	49.9	...	...
6	Cardiac insufficiency; chronic myocarditis; aortic regurgitation; right bundle branch block; Myocardia infarction; pulmonary embolism	3/25/21	Before oxygen...	24.56	15.23	96.0	53.4	28.54	154.3	40.3	48.2	...
			5 min. after oxygen...	27.99	13.60	98.1	47.8	(28.54)	(154.3)	41.3	49.9	Oxygen for one-half hour
			No oxygen...	23.34	15.33	88.3	58.0	26.45	143.0	42.7	63.8	Patient bled 300 c.c. day previous
		3/29/21	Oxygen...	19.14	14.53	90.7	69.0	21.10	114.0	39.0	45.2	...
			No oxygen...	16.20	16.20	88.0	74.5	21.79	117.6	43.5	46.5	...
			Oxygen for 45 min.	...	...	...	...	(21.79)	(117.6)	43.0	...	...
		10/27/20	Before oxygen...	16.38	...	76.1	...	21.50	116.3	39.2	...	Cyanosis +++
			Before oxygen...	...	9.43	...	43.8	(21.50)	(116.3)	...	52.2	Cyanosis +++
			Oxygen for 40 min.	20.14	...	97.7	...	20.60	111.2	45.7	...	Cyanosis ++
		10/28/20	Oxygen for 2 hrs.	...	12.14	...	56.0	(20.60)	(111.2)	...	55.2	Cyanosis +
7	Cardiac insufficiency; chronic myocarditis; aortic regurgitation; right bundle branch block; Myocardia infarction; pulmonary embolism	2/10/21	Oxygen of 2 hrs.	19.14	10.01	100.0†	53.6	18.70	101.0	75.0	82.4	Cyanosis relieved by oxygen
			Oxygen for 45 min.	...	...	...	...	...	...	...	...	...
			Before oxygen...	...	0.06	...	0.3	19.88	107.2	...	63.4	Cardiac failure
		2/11/21	Before oxygen...	...	...	...	...	...	...	...	...	...
			Before oxygen...	...	...	...	...	...	...	...	...	...
			Before oxygen...	...	...	...	...	...	...	...	...	...
		2/11/21	Before oxygen...	...	...	...	...	...	...	...	...	...
			Before oxygen...	...	...	...	...	...	...	...	...	...
			Before oxygen...	...	...	...	...	...	...	...	...	...
			Before oxygen...	...	...	...	...	...	...	...	...	...

The term "before oxygen" refers only to the day of the blood determination. It indicates that the blood for analysis was drawn before any oxygen therapy of the day, and that oxygen was subsequently given on the same day. "Oxygen for — min." indicates that the blood was taken immediately or a short time after oxygen therapy. All other terms as well, such as "no oxygen," refer solely to the day of the determination. For the precise relation of oxygen inhalation to the blood determination, as well as for the complete duration of the therapy, the text must be consulted. The parenthesis () about the figure for the oxygen capacity indicates that the determination preceding was used.

† There was apparently an excess of oxygen in physical solution, 0.44 vol. %.

cases of right bundle branch block, one with and one without auricular fibrillation, a decreased notching and a diminished height of the R wave was present during the inhalation of oxygen.

The question of the effect of oxygen on renal function is being additionally investigated. No definite action on the quantity of urine eliminated was discerned in the short periods in which oxygen was given.

SUMMARY

1. In a normal man, the inhalation of oxygen for one-half hour caused an increase in the oxygen saturation of the arterial and venous blood. In a second normal individual, the inhalation of oxygen for the same period caused a very slight rise in the venous saturation, the arterial saturation not being tested. The pulse was slowed in both cases. No significant changes occurred in the blood pressure, vital capacity, electrocardiogram, venous carbon dioxid content, or rate of respiration.

2. In seven cases of cardiac insufficiency, an anoxic (arterial) anoxemia was present in all, a stagnant (venous) anoxemia in all except one.

3. Oxygen inhalation regularly increased the arterial saturation. Where the anoxic anoxemia seemed due to passive congestion and edema at the bases of the lungs, the arterial saturation was raised to the normal by inhalation of oxygen for one-half hour. In the cases complicated by widespread pulmonary edema, relief of arterial anoxemia was accomplished in from forty-five minutes to two hours.

4. Oxygen inhalation increased the venous saturation in all except one case of auricular fibrillation. The elevation of the venous saturation was largely due to the raising of the arterial saturation. In a few cases, there was an additional and somewhat permanent increase in the venous saturation that seems best explained on the basis of an improved blood flow resulting from the increased supply of oxygen.

5. The arterial anoxemia of acute and chronic bronchitis, and emphysema, occurring in cardiac insufficiency, was fully relieved by oxygen inhalation. The venous saturation was correspondingly elevated.

6. The relief of the cyanosis and the slowing of the pulse were the outstanding objective changes. The blood pressure, vital capacity, arterial and venous carbon dioxid content, urinary excretion, and rate of respiration showed no definite changes from short periods of oxygen inhalation. The electrocardiogram showed consistent changes in two cases of right bundle branch block, no change in one uncomplicated

case of auricular fibrillation. Subjectively, the patients usually said they felt more comfortable or that their breathing was better, but they were rarely enthusiastic.

We wish to express our thanks to Dr. James H. Means for his invaluable aid during the work reported in this and the following two papers, and for his kind assistance in the preparation of the manuscript. We are greatly indebted to Dr. Donald D. Van Slyke and Dr. William C. Stadie who showed us the combined method of gas analysis before it was published, and to Dr. Paul D. White for his aid in obtaining and analyzing the electrocardiograms.