CERTAIN PHYSIOLOGICAL PRINCIPLES UNDERLYING RESUSCITATION AND OXYGEN THERAPY

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The vast body of knowledge concerning respiration stands in contrast to the lack of organization and equipment for the initiation and maintenance of adequate breathing. This criticism is applicable primarily to hospital practice since well drilled rescue squads have performed excellent service in the field treatment of gas poisoning.

Promising advances, however, in respiration therapy have been afforded by the studies and treatment of apnea neonatorum as sponsored by Eastman in Baltimore, Krieselman in Washington, Yandell Henderson and P. J. Flagg.

These efforts place credence in the concept that the initiation and maintenance of proper breathing in the infant at birth can be the routine and one of the truly life saving services performed by the physician. The realization of this concept depends upon the development of a standard procedure which awaits at the present time the resolution of conflicting ideas and methods of technic.

The solution of the problem will depend largely upon the activity of the anesthetist who already has assumed leadership and responsibility for organization and measures underlying adequate resuscitation and oxygen therapy. It is appropriate, therefore, to outline a few physiological principles familiar to many members of the Society, and yet too frequently overlooked in their application.

Effect of Carbon Dioxide in Relation to Intact Medullary Centers Governing Respiration.—Consider an experimental setup (1) in which

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a dog anesthetized with sodium diethylbarbiturate rebreathes in a closed system without provision for the absorption of carbon dioxide but with provision for the maintenance of normal oxygen pressure.

As the carbon dioxide pressure increases the blood pressure begins to fall and over a period of thirty minutes may reach a level of 100 mm. as compared with an initial level of 140 mm. The carbon dioxide percentage in the lungs at this point is about 20.

As the rebreathing continues to elevate the carbon dioxide pressure, a reversal in the blood pressure curve is signalized by a sharp rise which may reach a level between 156 mm. and 192 mm. The alveolar carbon dioxide pressure at this point is 230 mm. or about 30 per cent.

From this asphyxial peak blood pressure now rapidly declines to zero as cardiac failure supervenes.

Respiration until blood pressure begins the second fall is stimulated as shown by an increased depth and minute volume of breathing. As the blood pressure begins the final precipitous decline from the peak level, the respiratory excursions gradually decrease in rate and depth until cessation occurs. Circulatory failure follows within one to three minutes. Paralysis of the medullary centers has been brought about by the cumulative action of carbon dioxide which reached a pulmonary value of 30 to 35 per cent.

Following failure, resumption of respiration can be effected by only one or two manual compressions of the thorax, provided that the excess carbon dioxide can escape. The recovery of the normal respiratory rhythm then follows the reverse of the pattern that culminated in failure.

This type of experiment demonstrates (a) that percentages of carbon dioxide as high as 20 may stimulate temporarily the intact respiratory center in the anesthetized dog, (b) that percentages of carbon dioxide above 30 are associated with gradual depression ending in respiratory failure, and (c) the initiation of respiration following failure, provided that the carbon dioxide pressure is allowed to fall rapidly, occurs with only the little reflex stimulation associated with two or three manual compressions of the thorax.

In additional tests on the anesthetized dog, a concentration of carbon dioxide in the alveolar air maintained at 10 per cent stimulated respiration for a period of one and one half to three hours without depressing the blood pressure.

Murphy and Drinker (2) have pointed out the beneficial effects of 10 per cent carbon dioxide in contrast with 5 per cent carbon dioxide in the treatment of carbon monoxide poisoning in cats. Apart from the inherently valuable action of carbon dioxide in promoting a more rapid dissociation of carbon monoxide from hemoglobin, these experiments indicate the effectiveness of carbon dioxide under conditions in which severe damage to the medullary centers had not occurred. Of great im-
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Importance is the fact that in severe poisoning neither the 5 per cent nor the 10 per cent mixtures was effective.

Since the pendulum swing is away from the administration of carbon dioxide, it may be well to emphasize again (3) that carbon dioxide is an effective physiological agent in bringing about not only increased pulmonary ventilation but also augmentation of cerebral blood flow.

In man Drinker (4) has called attention to the fact that the inhalation of 93 per cent oxygen combined with 7 per cent carbon dioxide has been correlated with a lower death rate from carbon monoxide poisoning in New York City.

One must distinguish, however, between the field treatment of carbon monoxide poisoning in which the manual method of resuscitation requires the stimulatory effect of carbon dioxide and hospital practice in which appliances are at hand for effective ventilation of the lungs.

In a recent submarine test 2 per cent carbon dioxide in the atmosphere was well tolerated for a period of twenty-four hours. In simulated altitude tests Dill (5) has shown that 3 per cent carbon dioxide served to ameliorate the symptoms of mild anoxia mainly by increasing pulmonary ventilation, although the beneficial effect of increased cerebral blood flow cannot be overlooked.

Effect of Carbon Dioxide in Relation to Injured Medullary Centers.

In dogs anesthetized with sodium diethyl barbiturate, oxygen at a pressure of four atmospheres induces respiratory failure (6). Cessation of cardiac contractions, however, may be delayed for a period as long as one and one half hours after the termination of breathing.

In contrast with the toxic effect of high concentrations of carbon dioxide, oxygen inhalation at four atmospheres' pressure is associated with a convulsive type of breathing characterized by increased periods of apnea broken by irregular, inspiratory gasps.

Respiratory failure induced by the high oxygen pressure can be prevented by the maintenance of an alveolar carbon dioxide tension of 22 mm., conveniently carried out in a Drinker respirator. If, on the other hand, the carbon dioxide pressure is maintained at 65 mm., convulsive respiration supervenes early.

The conclusion drawn from these tests is that damage to the respiratory centers brought about by high oxygen pressure is enhanced by carbon dioxide tensions which are otherwise innocuous or actually stimulating.

Injury Induced by Low Oxygen Pressure.—Subjecting dogs to asphyxia by the inhalation of pure nitrous oxide, Eastman, Dunn, and Kreiselman (7) showed that resuscitation utilizing tank oxygen promoted a better recovery of blood pressure and respiration than the employment of a mixture of 90 per cent oxygen and 10 per cent carbon dioxide.

Asphyxia of this type is essentially an acute anoxemia and respiratory paralysis is brought about by anoxia. It is necessary to bear in
mind that the initial stimulation of respiration brought about by oxygen lack is essentially an acid effect on the chemoreceptors of the carotid body (8). Oxygen want is in no sense a true stimulant, and it induces physiological response only as a result of injury.

The conclusion drawn from these tests is that carbon dioxide acts as a depressant rather than a stimulant in the presence of severe injury to the medullary centers.

**Oxygen and Carbon Dioxide Content of the Blood During Respiratory Failure.**—Consider again a condition of respiratory paralysis brought about by the toxic action of oxygen at a pressure of four atmospheres. In one particular experiment arterial blood which was drawn fourteen minutes after the dog stopped breathing contained 6 volumes per cent of oxygen in physical solution or only one volume per cent less of oxygen than was present in the blood during normal respiration.

At the end of thirty-three minutes following respiratory failure, the hemoglobin of the venous blood was unreduced indicating that by diffusion alone and without the necessity of respiratory movement, conditions of equilibrium were nearly attained between the pressure of oxygen in the spirometer and the oxygen pressure in the blood.

With respect to carbon dioxide, however, the pressure in the venous blood rose from an initial value of 54 mm. to a value of 135 mm. at the end of the thirty-three-minute period of apnea. These figures indicate that carbon dioxide cannot be adequately eliminated from the lungs without pulmonary ventilation. The presence of pure oxygen in the lungs, on the other hand, assured complete oxygenation of the blood, although respiratory movements were at a standstill.

**Duration of Artificial Respiration Required to Effect Spontaneous Breathing.**—In experiments on the anesthetized dog in which respiration was temporarily paralyzed by oxygen administration at four atmospheres of pressure, there appeared to be a relationship between the duration of apnea and the time required for artificial respiration. Resuscitation in one experiment was begun thirty minutes after the onset of apnea. At the end of nineteen minutes of artificial respiration in the Drinker respirator, spontaneous breathing had not yet begun. An additional twenty-minute period of mechanical breathing was necessary to establish a normal respiratory rhythm.

**Technic of Artificial Respiration. Manual Methods.**—The Schäffer method combined with Nielson’s armlift (9) requires little discussion in this paper. The prone pressure method has become standard in emergency field practice and individuals have been kept alive for a period as long as twelve hours in the absence of normal breathing.

The method is far from efficient, however, when one considers that experienced operators exert as much as 100 pounds pressure on the lower rib cage at the rate of twelve to fifteen times per minute in order to effect a tidal air exchange of 600 to 800 cc.

**Mechanical Appliances.**—The recent reintroduction of mechanical
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devices after a bad start in 1744 and a continuously poor showing in unskilled hands merit careful comment.

In 1924 Professor Thunberg developed a mechanical appliance for artificial respiration known as the barospirator. In the description by Drinker (10) the barospirator functions as a cylinder completely to enclose the patient (Fig. 1). Ventilation is accomplished by pressure variations of 55 mm. of mercury at the rate of twenty-five strokes per minute. These pressure pulsations serve to move air in and out of the lungs without the necessity for volume changes in the pulmonary air spaces.

Barach (11) has recently applied the barospirator principle in the treatment of advanced pulmonary tuberculosis. Since resistance to air flow in and out of the lungs permits some compensatory chest movement relative to cyclic pressure change, an ingenious modification was made to equalize pressure on both sides of the chest wall and diaphragm to bring about a complete arrest of lung movement. Without equalization, positive and negative variations in pressure of 55 mm. of mercury produced a difference in pressure of about 5 cm. of water on the two sides of the chest wall. This consideration is highly important not only with reference to the arrest of lung movement but also in the prevention of lung injury from too great a differential pressure within and without the thoracic space.

If the barospirator is now modified so as to envelop the patient’s body with the head protruding through a rubber collar to the atmosphere (Fig. 2), then the principle underlying the operation of the Drinker and the Emerson respirators can be illustrated. For the maintenance of artificial respiration cyclic negative pressure of 10 to
15 mm. of mercury around the chest permits normal atmospheric pressure to expand the lungs without muscular effort. Expiration occurs passively when during a cycle the pressure is allowed to return to normal in the cylinder. By means of this appliance patients have been kept alive for as long as six and one half years.

Wilson (12) has pointed out that this type of mechanical respirator will be of aid in the treatment of poliomyelitis only when there is paralysis of the intercostal muscles or diaphragm. It will not help in cases of "bulbar" poliomyelitis in which the respiratory centers have been injured or in cases of obstruction to respiration brought about by pharyngeal paralysis.

With respect to the operation of this type of appliance, two facts are of particular significance, (a) positive pressure is not necessary for the expiratory phase of the cycle, and (b) the degree of effective negative pressure acting on the body is as great for a premature baby as for an adult.

Evidence of Damage to the Lungs.—Of prime importance is the consideration whether or not this appliance damages the lungs. Wilson (12) has described postmortem changes of emphysema and varying amounts of congestion and bronchopneumonia in patients treated in the respirator. Histologically the findings of emphysema and of serum and cellular transudation into alveoli are attributed to the use of the respirator. Although these postmortem changes may be terminal and induced by the use of excessive pressures, it is clear that injury may be associated with the use of this equipment.

Intratracheal Insufflation.—In 1909 Meltzer and Auer (13) maintained continuous respiration without respiratory movements in the dog by passing a continuous stream of air in one direction into the trachea by means of a catheter of such size as to provide for a return flow.
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From this technic has developed not only the endotracheal practice of administering anesthesia but also a method of resuscitation associated with the work of Flagg (14).

In 1924 Gwathmey (15) called attention to the value of insufflation of air or oxygen as a method of artificial respiration and stated that patients could be kept alive for periods as long as seven hours without a single respiratory movement being made.

Insufflation as practiced by Meltzer and Auer demonstrated that the blood could be oxygenated by the stream of air but that some increase in alveolar carbon dioxide could take place in the absence of respiratory movement.

In comparison with other lung gases it is necessary to distinguish between the relatively rapid diffusion of carbon dioxide through the tissues and the slow diffusion of this gas through the medium of the pulmonary spaces. As in the experiment on the dog previously described, diffusion of oxygen sufficient to maintain a normal percentage of oxyhemoglobin is not associated with an adequate loss of carbon dioxide from the lungs in the absence of respiratory movement.

Positive Pressure or Inflation Appliances.—Periodic inflation of the lungs by means of a mask and airway distinct from insufflation, is usually the only method of resuscitation feasible for the general practitioner.

Insofar as expansion of the lungs is concerned, there is no difference between a decrease in pressure around the chest wall as in the Drinker respirator or inflation of the lungs through a mask or catheter. Under both conditions a positive pressure force expands the lungs.

An essential consideration is the amount of pressure required for effective ventilation. The factor of pressure, moreover, is of no significance unless one considers the time factor. A pressure of 15 mm. of mercury, for example, applied in alternate three-second cycles, will not produce the distention associated with the same pressure applied in six-second cycles, although the total gas exchange is the same.

Danger of Overdistention of the Lungs.—In the submarine escape drill men were seriously injured in the early years of training as a result of too rapid ascent to the surface (16, 17). The cause of these accidents was found to be air embolism brought about by an overdistention of the lungs from an excess of intrapulmonic pressure.

In actual measurements during rapid ascent I have found intrapulmonic pressures to be as high as 60 mm. of mercury. Although the individual was protected by an ambient hydrostatic pressure of 15 inches of water, still the effective force tending to distend the lungs was about 30 mm. of mercury.

It is interesting to know that too rapid ascent accompanied by breathholding brings about an uncomfortable sensation of substernal stretching or the same symptom that accompanies excessive inflation of the lungs in healthy men. It is possible to ascend from a depth of 100
feet with the lungs filled with compressed air at four atmospheres of pressure to the surface simply by venting the lungs to prevent overdistention. Death, on the other hand, has followed too rapid ascent in conjunction with breathholding from depths of only 15 feet.

In corroborative experiments on dogs pressures of 80 mm. of mercury maintained for ten seconds were sufficient to cause air embolism (18). If overdistention of the lungs was prevented by bandaging the dog’s chest, this high pressure could be tolerated.

The principle of importance in these paragraphs is the danger of overdistention of the lungs which may be more readily brought about in the unconscious, relaxed patient than in the healthy individual who tends to resist excessive inflation by muscular splinting. The sensation elicited by overdistention of the lungs is substernal distress.

Tests Conducted on Healthy Men.—While tests performed on healthy men are open to a number of objections, yet with respect to the proper amount of inflation of the lungs a fairly reliable estimate may be made by using trained subjects.

Employing a Kreiselman resuscitator affording manually controlled, intermittent positive pressure, it was found that pressures of 20 mm. to 25 mm. of mercury were too great when applied in alternate five-second cycles to inflate the lungs of subjects in the supine position. Under these conditions substernal distress was a complaint.

Pressures, however, of 10 to 15 mm. of mercury applied for alternate five-second periods were adequate and well tolerated. While there is considerable fluctuation in the values of Table 1, a comparison of

### Table 1

Respiratory Minute Volumes of Healthy Men in the Supine Position Breathing Normally, and During the Inflation of the Lungs with Positive Pressure at the Rate of 6 Cycles per Minute, Duration of Pressure Force 5 Seconds

<table>
<thead>
<tr>
<th>Subject</th>
<th>Inflation Pressure, mm. Mercury</th>
<th>Normal M.V.</th>
<th>Normal Resp. R.</th>
<th>Vital Cap.</th>
<th>Tidal Plus Complementary Air</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
<td>15</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>11,400</td>
<td>17,100</td>
<td>18,300</td>
<td>7,700</td>
<td>9</td>
</tr>
<tr>
<td>B</td>
<td>13,100</td>
<td>16,900</td>
<td>24,800</td>
<td>7,810</td>
<td>95</td>
</tr>
<tr>
<td>C</td>
<td>10,200</td>
<td>16,000</td>
<td>10,000</td>
<td>13,500</td>
<td>10</td>
</tr>
<tr>
<td>D</td>
<td>8,300</td>
<td>11,300</td>
<td>12,000</td>
<td>10,000</td>
<td>10</td>
</tr>
<tr>
<td>E</td>
<td>8,300</td>
<td>10,600</td>
<td>14,900</td>
<td>10,400</td>
<td>9</td>
</tr>
<tr>
<td>F</td>
<td>10,800</td>
<td>13,200</td>
<td>16,000</td>
<td>10,700</td>
<td>12</td>
</tr>
<tr>
<td>G</td>
<td>14,800</td>
<td>15,100</td>
<td>14,200</td>
<td>15,300</td>
<td>13</td>
</tr>
<tr>
<td>Average</td>
<td>11,000</td>
<td>14,300</td>
<td>17,100</td>
<td>10,800</td>
<td>10</td>
</tr>
<tr>
<td>Tidal Volume</td>
<td>1,830</td>
<td>2,400</td>
<td>2,850</td>
<td>1,080</td>
<td></td>
</tr>
</tbody>
</table>

normal minute volume output of expired oxygen with the minute volume output during artificial respiration indicates values of the same order.
Inflation Followed by Manual Compression of Epigastrium to Aid Expiration.—In Figure 3 the average values for residual, supplemental, tidal, and complemental air measured at room temperatures are shown graphically for the group of men who served as test subjects.

The most efficient type of ventilation is a respiratory excursion that approaches as closely as possible the vital capacity. It has been found in our laboratory, for example, that six deep breaths per minute for one minute will remove almost all of the residual nitrogen from the lungs when oxygen is inhaled. During a period of three minutes all of the residual nitrogen can be replaced by oxygen.

With inflation of the lungs by positive pressures up to 15 mm. of mercury followed by passive expiration the supplemental air is not immediately affected. In order to increase the effectiveness of the removal of nitrogen from the lungs as well as to counteract any possibility of pulmonary overdistention, the diaphragm was pushed upward during expiration by exerting pressure on the epigastrium.

With the subject in a supine position, little good was accomplished by this movement. However with the subject lying on his side, my colleague, Lieutenant T. L. Willmon (MC), U. S. Navy, demonstrated an
appreciable increase in expiration employing the manual maneuver. As shown in Figure 3, the cycle of respiration now included part of the supplemental air. An average increase of 4.4 liters per minute was effected by pushing the diaphragm upward during expiration when the distending pressure was 10 mm. of mercury, maintained for five seconds. (Tables 1 and 2.)

### TABLE 2

**Respiratory Minute Volumes of Healthy Men Lying on the Side During the Inflation of the Lungs with Positive Pressure Followed by Manual Compression of the Diaphragm During Expiration**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Inflation Pressure, mm. Mercury</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>A</td>
<td>18,700</td>
<td>25,400</td>
</tr>
<tr>
<td>B</td>
<td>13,300</td>
<td>19,400</td>
</tr>
<tr>
<td>D</td>
<td>10,100</td>
<td>12,400</td>
</tr>
<tr>
<td>E</td>
<td>12,100</td>
<td>16,100</td>
</tr>
<tr>
<td>F</td>
<td>19,000</td>
<td>21,500</td>
</tr>
<tr>
<td>G</td>
<td>17,200</td>
<td>19,400</td>
</tr>
<tr>
<td>Average</td>
<td>17,400</td>
<td>17,400</td>
</tr>
<tr>
<td>Average Tidal Exchange</td>
<td>2,570</td>
<td>2,900</td>
</tr>
</tbody>
</table>

The Employment of Negative Pressure in Resuscitation.—If adequate pulmonary ventilation can be brought about by positive pressure inflation or by the principle underlying the operation of the Drinker respirator, there is no need to employ negative pressure to facilitate expiration.

The action of suction resulting in pulmonary injury was a prime objection to the use of the pulmotor. Negative pressure applied to the lungs, which are essentially capillary beds filled with blood, may lead to congestion and to an increased tendency to edema and hemorrhage into the alveoli.

Barach (19) has shown the advantage of positive pressure up to 8 cm. of water in the prevention and treatment of pulmonary edema. The most tangible reason underlying the value of this treatment is an actual “splinting” effect on pulmonary capillaries brought about by pressure. Conversely it follows that negative pressure has the reverse effect so that a condition of partial tracheal obstruction is simulated.

Coryllos (20), on the other hand, did not detect injury in dogs subjected to alternate positive and negative pressures of 14 and 9 mm. of mercury, respectively.

In a test conducted in our laboratory, a healthy man was subjected to alternate positive and negative pressure variations of about 8 mm. mercury by means of an Emerson resuscitator for a period of six hours. A rate of five respiratory cycles per minute was maintained throughout the entire period.
Following the test run there was no subjective or objective evidence, including roentgenologic examination, of pulmonary injury. This test indicated that the healthy lung may not be adversely affected by the pressures employed.

Extensive experiments are required, however, to determine the effect of cyclic negative pressure on the injured lung. The burden of proof that negative pressure is necessary rests with those who advocate its use.

**Summary and Clinical Application of Principles.**—The prime immediate need in resuscitation is to get oxygen into the lungs and to remove the inert nitrogen. Once the lungs are filled with oxygen, the hemoglobin will be adequately saturated without the need for respiratory movements. The problem then becomes one of merely maintaining sufficient pulmonary ventilation to prevent accumulation of carbon dioxide.

In hospital practice effective pulmonary ventilation can be accomplished by inflation of the lungs with pure oxygen using positive pressure not in excess of 15 mm. of mercury and in cyclic periods of five seconds’ duration. The inflation pressure can be reduced to about 10 mm. of mercury after three minutes, provided that essentially pure oxygen is used. Inflation has now accomplished its immediate purpose of the introduction of oxygen and the removal of nitrogen from the lungs. Continued artificial respiration seeks only to prevent carbon dioxide accumulation.

The danger inherent in the use of mechanical appliances for respiration consists in overdistention of the lungs with excessive positive pressure, and in the employment of negative pressure to effect suction of expired air from the lungs.

With the patient lying on his back the satisfactory introduction of oxygen into the lungs implies the use of a properly fitted airway which is as essential to the success of resuscitation as is the availability of oxygen.

Removal of secretions from the oropharynx by slight postural inclination and aspiration is, of course, the routine practice of the anesthetist.

Measures to keep the patient warm are frequently neglected. In emergency field treatment incident to naval casualties, hot towels placed over the upper abdominal and hepatic areas have provided an effective supply of heat.

**Treatment of the Newborn.**—The employment of resuscitation in hospitals finds its greatest application in the treatment of apnea neonatorum. Whether the cause of the apnea is cerebral hemorrhage, narcosis, or anoxia, the treatment consists of introducing oxygen into the lungs. Where formerly vigorous manual methods of manipulation were employed to initiate breathing, organized hospital procedure now calls for meticulous care in handling the infant, application of warmth,
aspiration of mucus to replace the injurious gauze sponge, and introduction of oxygen into the lungs.

The immediate administration of carbon dioxide with oxygen does not appear to be necessary. Pecul blood studies with reference to carbon dioxide content (21), and although showing variation of carbon dioxide tension (22), make it clear that carbon dioxide is accumulating in the tissues and blood of the apneic infant as in the apneic dog. Certainly acapnia does not exist.

It should be stressed that the grave danger of cerebral hemorrhage is augmented by anoxia which leads to increased permeability of the capillary wall and the development of perivascular edema and petechial hemorrhages (3). Another factor tending to produce cerebral hemorrhage is the asphyxial rise in blood pressure. In the experiment on the dog previously discussed in which the oxygen supply was adequate during the period of carbon dioxide accumulation, the blood pressure reached high levels.

With a mechanical appliance for inflation at hand, any attempt to stimulate the respiratory center with carbon dioxide must give way to the immediate introduction of oxygen into the lungs. Inflate the lungs with oxygen and the carbon dioxide will take care of itself.

Data, however, are lacking on the important problem as to how much pressure is required for the inflation of the lungs of the newly born. The anatomical considerations underlying this problem should be stressed. In contrast with the adult lung, one deals essentially with atelectatic gland-like structures that completely fill the thorax. Under these conditions intrathoracic pressure is said to be absent and the lungs empty almost completely with each expiration. It is likely that the same pressure, 10 or 12 mm. of mercury, required for the adult, will be adequate and not injurious to the infant lung.

The best method of procedure for resuscitation of the infant is a controversial subject. Kreiselman places the newly born infant in a warm bassinet and, after removing obstructive secretions by gentle aspiration, administers artificial respiration by intermittent inflation of the lungs with pure oxygen, using pressures not in excess of 12 mm. of mercury.

The endotracheal insufflation method of Flagg (23) based on surgical principles would appear to require specially trained operators. Utilizing this method McGrath and Kuder (24) report excellent results in conjunction with the employment of oxygen-carbon dioxide mixtures.

The time factor, however, demands the same urgency in the treatment of asphyxia as in the arrest of hemorrhage, and hence, simplicity of technic becomes a dominant consideration.

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There is no need to review material from the comprehensive paper of Warnock and Tovell (25). I desire to stress, however, certain experiences connected with the administration of oxygen to healthy men.
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Facilities for Oxygen Administration.—It has been difficult to assemble equipment for oxygen inhalation that could be worn either for long periods of time or on successive days by the same individual. The crux of the setup is the individual's connection with the source of oxygen supply.

A mouthpiece could be tolerated for about an hour. Masks have been worn for periods of four to twelve hours but considerable pain has been experienced by some individuals over the bridge of the nose.

Our problem has been solved by the fabrication of a rubber helmet which could be placed in the circuit of a closed system consisting essentially of a rubber bag, coiled canister containing carbon dioxide absorbent, and a spirometer for measuring oxygen supply (26).

By means of this system men have breathed 99 per cent oxygen continuously and comfortably for periods as long as seventeen hours. Changes in the type of equipment from hood to mask are frequently of help. As in anesthesia, success in oxygen therapy depends upon close supervision and meticulous attention to detail in administration.

Tolerance for High Oxygen Concentrations.—There are some individuals who either are or can become sensitive to oxygen (26). One of our divers developed an idiosyncrasy to oxygen as a result of repeated exposures at a pressure of two and one-half atmospheres. In contrast with the usual blanching of the face when oxygen is breathed at high pressures, an erythema of the face and neck developed even when oxygen was inhaled at atmospheric pressure. The subsequent development of an allergic type of dermatitis was relieved by the administration of histaminase (Torantil, Winthrop).

The tolerance of patients for high percentages of oxygen may be greater than that of healthy men, rabbits, dogs, and mice. It would appear to be difficult, however, to determine under what conditions oxygen itself is toxic when administered to patients. The lung injury brought about by oxygen may be indistinguishable from the condition for which oxygen is administered.

The safe procedure would be to utilize the experience derived from tests on lower animals and on healthy men. This experience calls for the limitation of oxygen to percentages of 70 or below unless emergency cardiac therapy requires 99 per cent oxygen.

I refer, of course, to continuous administration, since temporary respite from high oxygen concentrations appears to minimize its toxicity.

Early Administration of Oxygen.—A typical error in therapy follows. An ambulatory patient complained of hoarseness following an accident in which gasoline was drawn into the throat. A mild degree of tracheal obstruction was not recognized until several hours later when the signs of pulmonary edema and cyanosis were manifest. Convalescence which might have required several days if early positive pressure oxygen therapy had been instituted was prolonged over a period of months; the heart was permanently injured.
It is beginning to be recognized that oxygen is a substance to be administered whenever the oxygen pressure in the lungs falls below normal. Barach (27) has rendered a valuable service for aviation in calling attention to the need for oxygen at altitudes of 10,000 feet and above. As the flying time has been prolonged the ceiling altitude for oxygen administration has been progressively lowered. Essentially it is not amiss to consider that even in healthy, selected men compensatory changes occur whenever the oxygen pressure drops below normal.

In conclusion I should like to emphasize a most important characteristic of gases, namely, the property of diffusion. The inhalation of pure oxygen adds about 2 volumes per cent of oxygen in physical solution to the blood. In measurements in dogs I found that each atmosphere added 1.8 volumes of oxygen in solution (6).

What is more important, however, than the oxygen content is the increased tissue oxygen pressure associated with the inhalation of high oxygen concentrations. Campbell (28) has shown that the inhalation of pure oxygen at a pressure of one atmosphere raises the pressure of oxygen in certain tissues about 30 mm.

While Exner's law governing diffusion of gases through liquids appears to be applicable to the diffusion of gases in the body, the following experimental data will make the phenomenon of diffusion more real. Some years ago at the Harvard School of Public Health the nitrogen dissolved in the tissues of anesthetized dogs was removed by means of oxygen inhalation through a tracheal cannula. For some time it was puzzling to note that nitrogen could be collected from the lungs for periods as long as fourteen hours. It was then suspected that atmospheric nitrogen was diffusing through incision openings and from these areas transported to the lungs by way of the blood stream. This surmise was verified when, following the careful closure of the incisions, nitrogen removal from the tissues was completed in from three to four hours.

Recent tests with helium have demonstrated further the manner of gaseous diffusion (29). If an individual's body is surrounded by a rubber bag, then helium will diffuse through the skin to be transported by the blood stream to the lungs. The helium diffusing into the lungs can then be collected in a closed system circulating air or oxygen. The cutaneous diffusion of helium in relation to temperature is illustrated by Figure 4.

The facts concerning diffusion serve to illustrate the value of a type of oxygen therapy not usually emphasized, namely, the exposure of chronic ulcers of the leg to an atmosphere of oxygen. In addition, however, these data on diffusion make clear the value of high concentrations of oxygen in the alleviation of muscular anoxia incident to acute coronary thrombosis.

The treatment of wounds with germicidal gases (30, 31) is a development of particular interest in this connection. The effectiveness
of this mode of therapy as well as the potential danger in using chemically active gases is based on the property of diffusion.

In conclusion, the most important consideration concerning the administration of oxygen is its early employment, utilizing comfortable and effective facilities. We have learned that this applies not only to the ward patient but also to the military aviator.

Fig. 4. Cutaneous diffusion of helium in relation to temperature, measured as cubic centimeters of helium recovered from the lungs per hour when the body is immersed in a helium atmosphere, pressure 700 mm. The numbers, 1 to 5, refer to different subjects. The encircled values were obtained after the previously heated ambient helium had been cooled to 29 C. (Reproduced from the American Journal of Physiology.)
REFERENCES


