POSITIVE PRESSURE RESPIRATION AND ITS APPLICATION TO THE TREATMENT OF ACUTE PULMONARY EDEMA *


The purpose of this paper is to present observations we have made which provide a physiologic basis for the use of positive pressure respiration in the treatment of acute pulmonary edema. For the most part positive pressure has been thought of as a method of resuscitation such as that accomplished by the pulmotor in accidental asphyxiation. The function of pressure in the respired air has, however, a broad physiological significance, being employed by the human organism itself as a compensatory mechanism as well as lending itself to therapeutic application in inhalational therapy. We wish to present the subject from the following points of view: (1) A critical discussion of the pertinent literature. (2) Animal experimentation on the development and treatment of acute pulmonary edema. (3) Physiological studies on the effect of positive pressure respiration in human subjects. (4) The clinical results of treatment with positive pressure in patients with acute pulmonary edema.

1. Discussion of Literature

In 1878 Welch 1 presented his theory of the origin of pulmonary edema in the following words: "A disproportion between the working power of the left ventricle and of the right ventricle of such character that the resistance being the same the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." By squeezing the left ventricle of rabbits between his fingers, Welch observed in many instances forcible contraction of the right ventricle with diminished force of the left ventricle, as indicated by the pressure in the carotid artery, with the result that well marked pulmonary edema took place.

Meltzer 2 brought apparent confirmation to this hypothesis by producing pulmonary edema in rabbits through the intravenous injection of adrenalin. He explained this occurrence as a result of the considerable constriction of the smaller systemic blood vessels, which presented such an increased burden to the left ventricle that it became unable to expel all the blood which it received from the pulmonary veins, while on the other hand the right ventricle unloaded with increased energy upon the lungs all the blood which the contracting vessels drove into it.

Haven Emerson 3 in 1909 showed that pulmonary edema produced by adrenalin could be consistently removed by applying artificial respiration

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through a tracheotomy tube, gently distending the lungs and allowing them to collapse. The explanation he advanced for the striking improvement in respiration and circulation which occurred was that the full expansion of the lungs due to distention from within forced a considerable amount of blood onward to the left auricle and ventricle; during expiration more room in the pulmonary vessels and a diminished resistance in the lungs allowed the distended right ventricle successfully to empty itself. He suggested as a clinical procedure artificial respiration, raising the arms of the patient above the head and then pressing them across the upper part of the abdomen, believing that this accessory pumping action would facilitate the flow of blood through the lungs.

This suggestion was tried several weeks later by Barringer, in a patient with cardiac insufficiency who suddenly developed edema of the lungs. At the end of an hour of artificial respiration the signs of edema, rattling in the throat and moist râles had largely disappeared.

In 1897 Norton had reported a case of edema of the lungs due to carboic acid poisoning in which a rapid clearance of the edema took place with the use of the Fell-O’Dwyer forced respiration apparatus. Although a theoretical discussion of the mechanism was not made in this report, the clinical result was carefully described and was unmistakably the result of the introduction of a laryngeal tube and the application of forced respirations under positive pressure. (Description of apparatus published by Northrup.)

The use of positive pressure as an aid to breathing is described in even earlier literature. Oertel (1878) employed 20 to 100 inspirations of air compressed to $1/10$ to $1/100$ atmosphere excess pressure in the treatment of severe asthma, and remarked that the dyspnea is relieved while the inflation of air cells is checked by the cessation of the forced inspiratory movements and the rarefaction of air within them prevented. He also had traced the secretion of sero-mucous fluid into the finer bronchi to the violent inspiratory dilatation of the thorax during occlusion of the bronchioles; a concept which our own studies appear to confirm.

The observations of Emerson as to the effectiveness of artificial respiration in abolishing pulmonary edema due to adrenalin were confirmed by Auer and Gates in 1917 and by Johnson. Auer and Gates also showed that tracheal stenosis accentuated the edema caused by adrenalin. When adrenalin was injected in rabbits whose hearts were exposed for inspection and in whom artificial respiration was carried out, they observed the pulmonary artery to be dilated, the left auricle enormously swelled, the left ventricle small, and sooner or later the rate of contraction of the left ventricle became only half that of the right side of the heart. However, despite the apparent fulfillment of the fundamental postulate of Welch’s theory, the degree of pulmonary edema produced was slight and even negligible when compared with the marked edema which resulted from the same dose of adrenalin injected into animals whose thorax was intact. Even more
striking edema was produced when the vagi had been divided. The authors rejected Emerson’s tentative explanation that distention of the lung by artificial respiration drove a considerable amount of blood into the left auricle and thus relieved the pulmonary congestion, nor did they believe that the edema resulted from back pressure from the left ventricle, since they did not observe any dilatation of the left ventricle or regurgitation in the left auricle. The left ventricle in the rabbit after adrenalin seemed to be in a state of greater tone than normal. They believed that artificial respiration with positive pressure did not exert its inhibitory action on pulmonary edema through action on the heart itself, but that the significant factor involved was the relief of the negative pressure within the chest which exerted a suction action, like dry cups, on capillaries in the alveolar walls.

Although adrenalin relieves bronchial asthma, it had been shown by Golla and Symes that adrenalin in animals produces constriction of the bronchioles unless previous constriction has been produced by other drugs. Since constriction of the bronchial muscles had been experimentally demonstrated as a result of adrenalin injection, Auer and Gates assumed that an increased negative pressure within the chest became necessary during inspiration, producing the cupping action on the alveoli which aided the passage of fluid from the engorged capillaries into the alveoli.

According to these authors, the positive pressure which artificial respiration produced in the lung partially overcame the bronchial constriction due to adrenalin and thus prevented the intra-alveolar pressure from becoming highly negative during inspiration, in that way removing the suction action on the pulmonary capillaries.

Loeb in reviewing the evidence just presented came to the conclusion that the reduction of the negative pressure due to insufflation of air into the lung was the important factor in the prevention or amelioration of pulmonary edema produced by adrenalin.

Plesch also made the suggestion that increased pressure in the air passages of the lungs would be valuable in the treatment of pulmonary edema. He mentioned that the effect would be to push the blood already in the pulmonary circuit onwards to the left ventricle and at the same time to oppose the delivery of more blood by the right ventricle; he believed it would be of special importance when the patient’s respiration was “rattling,” for this was considered by him to be a compensatory mechanism to hinder the edema; the patient makes short inspiratory gasps since the diminished pressure during inspiration is dangerous, tending to cause edema and makes prolonged rattling expirations through the bronchi and glottis which keep up a pressure acting in the opposite direction.

Poulton reported beneficial results from the use of this technic in some cases of paroxysmal dyspnea (“cardiac asthma”) and in bronchial asthma, although no benefit was obtained when there was generalized heart failure.

The production of congestion and edema of the lung as a result of tracheal stenosis was shown by Moore and Binger to be due to the obstruc-
tion during inspiration, for these changes did not take place during expiratory obstruction alone. Barach 15 confirmed these observations and also showed that expiring against a positive pressure created no significant changes in the lung, whereas inspiring against a negative pressure caused congestion and edema, particularly in the lower parts of the lung and areas of emphysema at the periphery. In animals breathing through constricted orifices the negative intrapleural pressure increased as high as tenfold the normal value during the course of a six-hour experiment but when respiration was conducted under a positive pressure of 5 cm. of water, a substantial reduction in the negative intrapleural pressure took place. This was more marked when a helium-oxygen mixture, in which the density was one-third that of oxygen, was employed.

The effect of increased negative pressure on the pulmonary blood flow has been the subject of considerable study, the literature having been reviewed by Tigerstedt 16 and by Wiggers.17 Daly 18 showed that expansion of the lungs in animals, accomplished by a negative pressure chamber, resulted in an increased pulmonary and peripheral blood flow. Mollgaard,19 in experiments on the whole animal found similar results. It appeared, therefore, that even relatively marked expansion of the lungs decreased the resistance of the pulmonary bed. When inspiratory obstruction was produced in the cat, Huggett 20 found that a marked increase in the minute volume of the heart took place, whereas expiratory obstruction caused the reverse, the blood flow being determined by the Ficke principle.

The sequence of events in the production of pulmonary congestion and edema due to tracheal stenosis may now be postulated as follows: There is an immediate increase in the negative intrapleural pressure which becomes progressively greater. The resistance of the pulmonary bed is lessened and there is at first an increase in the pulmonary and peripheral blood flow. An additional factor promoting increased filling of the right heart may be dilatation of the right auricle. As the intra-thoracic negative pressure increases, blood continues to enter the lungs through the right ventricle but the passage of blood through the lungs into the left auricle and especially from the left ventricle into the extra-thoracic aorta is hindered by the high negative chest pressure. A progressive accumulation of blood in the lungs follows, with a consequent increase in the capillary blood pressure causing a greater filtration pressure outward. Finally, the physical effect of a pathologically heightened negative pressure in the chest exerts a suction action on the capillaries resulting in an exudation of serum into the alveolar walls and spaces, and into the bronchiolar structures as well.

In another group of cases, pulmonary edema may be caused by an increase in permeability of the capillaries to edema fluid. Landis 21 found that when capillaries are deprived of oxygen for three minutes their permeability to protein is increased. Krogh 22 showed experimentally that dilatation of a capillary also increases its permeability. Since anoxemia and pulmonary engorgement are both frequently present in conditions in which pulmonary
edema may occur both these factors may participate. When pulmonary edema is caused by irritant gases such as chlorine in commercial plants and to phosgene in war gas poisoning, the pathogenesis of edema of the lungs may be traced directly to increased permeability. Pulmonary edema as a complication of pneumonia is probably in large part due to an increase in capillary permeability caused by inflammation, probably similar to the irritant inflammation of poisonous gases. However, in many patients with pneumonia the condition is complicated by left as well as right ventricular failure and it is at times difficult to say whether cardiac failure followed pulmonary edema or whether it was present as a contributory cause. An attempt will be made in the clinical section of this paper to analyze the various factors that may have been involved in individual cases of edema of the lungs.

In previous reports dealing with the effect of helium-oxygen mixtures in asthma and respiratory obstruction, Barach [1] pointed out that the use of positive pressure decreases the effort necessary for inspiration and that in patients with asthma the existence of positive pressure during expiration maintains a backward distending pressure which keeps open bronchial and bronchiolar structures that physiologically constrict during the expiratory cycle. This observation suggested the explanation of why patients with asthma and emphysema so frequently pursed their lips during expiration and arbitrarily increased the resistance to the egress of air. This mechanism, developed by the patients themselves, appeared to have the physiological advantage of keeping open bronchiolar passageways, thereby producing a more efficient emptying of the alveolar air. It was suggested that the expiratory grunt in lobar pneumonia was a similar protective mechanism. Furthermore, it was found that patients with more or less continuous asthma of moderate degree will frequently obtain marked relief of their wheezing when they follow the instruction to breathe through partially closed lips for 3 to 10 minutes. The râles in expiration will at times clear up immediately, apparently due to distending the bronchioles through internal pressure. This observation provided an additional stimulus to employ positive pressure respiration in the treatment of acute pulmonary edema; we reported in a preliminary communication three cases in which a swift clearance of the moist râles in the chest took place, even in the presence of advanced circulatory deficiency.

Since congestion and edema do not occur as a result of expiratory obstruction but consistently follow inspiratory obstruction, the use of positive pressure respiration receives additional support in the treatment of dyspnea due to obstruction. Inasmuch as excessive pressures would obviously prevent the entrance of an adequate amount of blood into the right heart, it was cautioned that this procedure should be followed only with the careful use of manometric readings of the pressure of the expired air.

In the review of the literature above, an essential factor in the production of pulmonary edema, due either to adrenalin or to tracheal stenosis, appeared
to be a heightened negative pressure within the chest exerting a direct suction action on the capillary wall. It is of some interest at this point to remember that Graham suggested that the swift formation of pleural exudates in influenza broncho-pneumonia might be due to a negative pressure within the chest produced by the attempt to inflate the lung through smaller bronchial passages that were constricted by inflammatory swelling.

In the earlier communication we reported the rapid clearance of acute pulmonary edema as the result of the continuous application of positive pressure during the total respiratory cycle. Before reporting these results in detail it was thought advisable to study the mechanism more carefully. Although the sequence of events in the production of pulmonary edema following tracheal stenosis seemed clear from the physiological data described above, the type of edema associated with circulatory failure was less easily explained. It seemed likely that additional light could be thrown on the pathological physiology of pulmonary edema due to left ventricular failure if more careful observations were made on experimental edema of the lungs in rabbits due to adrenalin.

2. Experimental Observations on the Development and Treatment of Acute Edema of the Lungs Caused by Adrenalin

Rabbits were anesthetized with evipal intravenously for short experiments and ether by the open drop method in long continued experiments. Adrenalin was injected into the ear veins, the dosage employed being 0.5 c.c. of a 1 to 1000 solution per kg. body weight. Within 15 seconds after the injection the majority of animals stopped breathing for a period of 15 seconds to 2 minutes. In some instances the rabbit died during this period before the development of edema. Autopsy then revealed massive pulmonary congestion. When the animal began to breathe again the respiratory rate was extremely rapid and shallow and generally within 2 to 5 minutes pulmonary edema could be clinically recognized, either by palpation or auscultation. Before the death of the animal a foamy, frequently blood-tinged, fluid exuded from the nostrils. Autopsy of the latter animals showed widespread pulmonary congestion and edema. The heart was markedly enlarged, the enlargement being due to a marked dilatation of the right ventricle and auricle. The left auricle was usually moderately dilated. The left ventricle was contracted and showed no evidence of dilatation.

Data included measurements of the intrapleural and intratracheal pressures, the pulmonary ventilation and tidal air, the systolic arterial pressure, venous pressure, pulse and respiratory rates. A total of 100 rabbits were used. All determinations could not be obtained simultaneously on each animal but there were at least 10 observations on each measurement described. A spirometer of small diameter, namely 5.08 cm., was built in order to show recognizable oscillations of the tidal air and measure the pulmonary ventilation of the rabbit. Each millimeter rise in the bell represented a volume
change of 1.96 c.c. A high speed drum was used to record graphically the changes in chest pressures as well as the respiratory tracings.

The arterial pressure was obtained by inserting a needle into the femoral artery and connecting it with a long glass tube containing saline with a small amount of oxalate solution. Venous pressure was measured in a similar way using the femoral or ear veins. Graphic recording of the intrapleural and intratracheal pressure was made possible by a delicate float with an attached pen suspended in a water manometer.

The roentgen-ray pictures were made possible by a special technic used by Dr. Ross Golden in which films could be taken at 10 to 15 second intervals. The rabbits were tied to a board and pictures taken before and at various intervals after injection and after application of positive pressure respiration.

A series of roentgen-ray pictures taken at 15 second intervals after intravenous injections of adrenalin revealed a progressive increase in the size of the heart shadow. This increase was observed as early as 10 seconds after the injection. In the accompanying reproduction (figure 1) it will be seen that the largest transverse diameter of the heart increased from 3.5 cm. before adrenalin to 3.8 cm. one minute after and 4.1 cm. three minutes after. In addition the lung field became progressively darker, indicating the development of pulmonary congestion and edema.

In figure 2 the size of the heart is shown after adrenalin, and after adrenalin with positive pressure. The rabbit was given the usual dose of adrenalin intravenously and the first picture taken one minute later. Positive pressure was applied immediately thereafter by intermittent inflation of the lungs at a rate of 36 times a minute. The lung was expanded by a pressure of 8 to 10 cm. of water, the trachea being connected to a basal metabolism apparatus in which a positive pressure blower was used. The rabbit breathed 100 per cent oxygen in this experiment, although in the majority air only was employed. Expiration was allowed to take place passively. One minute after the injection, the transverse diameter of the heart increased from 3.3 cm. to 4.1 cm. After three minutes of positive pressure breathing, the heart size was slightly smaller, 3.9 cm. in transverse diameter. The animal was killed five minutes later. Considerable passive pulmonary congestion was found but no evidence of edema.

Figure 3 shows the effect of intermittent inflation of the lung superimposed on a continuously exerted positive pressure both during inspiration and expiration. The animal's trachea was connected with a motor blower unit which maintained a positive pressure of 4 cm. during inspiration and 6 cm. during expiration. Intermittent inflation was then added so that the animal experienced a pressure of 10 cm. during inspiration and 6 cm. during expiration. The first photograph shows the normal transverse diameter of the heart to be 3.4 cm. One minute after injection of adrenalin there is an increase to 4.0 cm. The combined intermittent inflation and continuous positive pressure was begun immediately after the second picture and the film taken three minutes later. This showed a marked decrease in the trans-
Fig. 1. Effect of the intravenous injection of adrenalin on the size of the rabbit heart.
Fig. 2. Effect of intermittent inflation of the lung on the size of the rabbit heart after adrenalin.
Fig. 3. Effect of positive pressure on the size of the rabbit heart after adrenalin.
verse diameter of the heart to 3.1 cm. It will also be observed that the lung was expanded, the diaphragm flattened, and the lung field showed an increased radiability. The animal died five minutes later possibly due to the maintenance of excessive pressure interfering with an adequate inlet of blood into the right heart. At autopsy, however, pulmonary congestion and edema were not found.

The three pictures reproduced above illustrate the significant findings obtained by roentgen-ray of the heart. We may summarize these results as follows: Following the intravenous injection of 0.5 c.c. of adrenalin per kg. of body weight, there is a marked increase in the transverse diameter of the heart within 15 seconds. A further progressive increase takes place, reaching a maximum at approximately three minutes after injection. At this time a darkening of the lung shadow, particularly at the bases of the lung, takes place.

When positive pressure is applied by intermittent inflation of the lungs, pulmonary edema may be prevented. When moderate pressures are used, the heart size appears to be slightly decreased. Under these circumstances autopsy shows a dilated right ventricle, passive pulmonary congestion of moderate extent, without edema. When more marked positive pressure is employed, such as is achieved by intermittent inflation of the lungs plus a positive pressure continuously exerted during expiration as well as inspiration, the heart size may become even smaller than it was during the control period. Under these circumstances pulmonary congestion and edema may be prevented. However, the animal may die, if excessive restriction of blood flow is maintained for a long period.

We have not attempted to determine in a precise way the optimal pressures required to control the onset of pulmonary congestion and edema, but have established the fact that pulmonary edema may be prevented by the application of positive pressure respiration of such a degree as to cause a slight diminution in the size of the heart. The possibility presents itself that cardiac dilatation may be controlled by the application of positive pressure respiration in which a decreased entrance of blood into the right heart is accomplished. The danger of an excessive curtailment of total blood flow must of course be kept in mind.

Respiratory Measurements after Intravenous Injection of Adrenalin in the Rabbit

Since it had been assumed that a pathologically elevated negative chest pressure was the important factor in the production of pulmonary edema it seemed desirable to make direct observations of the intrapleural pressure. In the accompanying graph, the intrapleural pressure of a rabbit before and after adrenalin is shown (graph 1). It will be seen that the intrapleural pressure ranged from approximately — 1.6 to — 4.4 cm. of water during the control period. After injection of adrenalin (1.2 minutes) the range
was exceedingly small, namely about 0.3 cm., the average pressure being —2.4 cm. The respiratory rate increased from 55 to 175.

In graph 2, the intrapleural pressure of a rabbit is shown in which there is not only a decrease in the range of pressure but in which the average pres-

![Graph 1. Effect of adrenalin on the intrapleural pressure of a rabbit. Control 1.2 min. after adrenalin.]

sure between inspiration and expiration is even less negative than in the control period (graph 2). Thus, the mean negative intrapleural pressure is — 4.9 cm. before injection of adrenalin, — 2.8 cm. two and one-half minutes after injection and — 2.6 cm. five minutes after injection.

The changes produced by intermittent inflation of the lung in a rabbit which had previously been injected with adrenalin are shown in graph 3.

![Graph 2. Effect of adrenalin on the intrapleural pressure of a rabbit. Control 2.5 min. after adrenalin 5.0 min. after adrenalin.]

The tidal air was increased from 9.8 to 51 c.c., the pulmonary ventilation from 1176 c.c. to 1656 c.c., the intratracheal pressure from that of the atmosphere to as high as plus 6 cm. during the expanding or inspiratory cycle.

The intrapleural pressure rose (as a result of intermittent inflation) from a range of approximately — 2.0 cm. to — 3.2 cm. to a range of plus 0.2 cm. during inspiration and — 2.3 cm. during expiration.

A detailed view of the effect of continuous positive pressure, without intermittent inflation, may be seen in graph 4. The control period shows a tidal air of 5.9 c.c. and a pulmonary ventilation of 384 c.c. After the onset
of a continuous pressure of 2.0 cm. of water throughout the respiratory cycle, the tidal air was 7.8 c.c. and the pulmonary ventilation 546 c.c. Adrenalin was then injected, with positive pressure continuing. The tidal air dropped to 3.9 c.c. 14 minutes later with a pulmonary ventilation of 585 c.c. Twenty-

Graph 3. Effect of positive pressure respiration on a rabbit after adrenalin.
Normal respiration
Positive pressure respiration

seven minutes after injection of adrenalin, the tidal air was 11.8 c.c. with a pulmonary ventilation of 1300 c.c. Thirty-six minutes after adrenalin and one minute after pressure was withdrawn, the tidal air was 11.8 c.c. and the pulmonary ventilation 1240 c.c. The animal was autopsied. Pulmonary edema was absent. There was only slight pulmonary congestion. The heart did seem to be dilated.

Graph 4. Effect of positive pressure on the respiration of a rabbit after adrenalin.
We may summarize the results just reviewed as follows:

The characteristic effect of the intravenous injection of 0.5 c.c. adrenalin per kg. of body weight on the respiration of the rabbit is an immediate and marked increase in rate, as high as 175 per minute. The tidal air becomes exceedingly shallow, dropping as low as 1 to 2 c.c. In many instances there is a temporary period of complete cessation of respiration. The extreme shallowness of respiration undoubtedly introduces an anoxic factor, although measurements of the oxygen saturation of the arterial blood were not made. Since capillary permeability has been shown to be increased by anoxemia, this factor may play a rôle in the production of edema. 21

The significant finding in these experiments is that concerned with the modification of intrapleural pressure. These observations demonstrate that no increase in negative pressure takes place in the intrapleural space as the result of the injection of adrenalin. Observations were recorded on 75 rabbits. The main effect was a consistent and marked decrease in the range of intrapleural pressure. The mean point between inspiration and expiration was approximately the same as that in the control period. A pathological increase in the negative intrapleural pressure was only found shortly before death, about 5 minutes after onset of pulmonary edema. At this time the tracheal tree was filled with foaming, blood-stained mucus, the animal resorting to powerful inspiratory gasps in order to suck air into his lung.

The effect of positive pressure whether applied continuously during inspiration and expiration or whether administered with intermittent inflation of the lung was to raise the intrapleural pressure so that it was atmospheric at one phase of the respiratory cycle and approximately — 2 cm. at the other phase.

**Effect of Positive Pressure Respiration on the Systolic Arterial Pressure and the Venous Pressure in Rabbits after Adrenalin Injection**

The systolic arterial pressure was measured by cannulizing the femoral artery and connecting it with a water manometer containing normal saline; the venous pressure was obtained in the same way. Fifteen rabbits were used. The procedure was similar to that employed in arriving at the previous measurements. Determinations were made on the systolic arterial pressure and the venous pressure before and after injection of adrenalin, with and without positive pressure. The results may be summarized in the following charts (charts 5 and 6).

In chart 5 it will be seen that immediately following the intravenous injection of the standard dose of adrenalin, a rise in systolic arterial pressure took place from 79 mm. Hg to 240 mm. Hg. (The pressure was measured in cm. of salt solution and converted into mm. of mercury by calculation.) The arterial pressure then declined, and, if the animal sur-
vived, approached the control level in 15 to 20 minutes. The course of a typical experiment is shown in the graph. The venous pressure generally showed a very slight rise, as shown in the graph, from 55.0 mm. of water to 65.0 mm. of water. If the animal died there was frequently a further rise of venous pressure of 10 mm. If the animal survived, the venous pressure fluctuated within a range of 10 mm. around the control level.

![Graph showing the effect of adrenalin on systolic arterial pressure and venous pressure of normal rabbit.](chart5)

**Chart 5.** Effect of adrenalin on systolic arterial pressure and venous pressure of normal rabbit.

In chart 6 a graphic record is shown of a rabbit breathing under positive pressure, injected with adrenalin, and intermittently treated with positive pressure afterwards. It will be seen that positive pressure respiration of 4 to 6 cm. had no noticeable effect on the systolic arterial pressure either before injection of adrenalin or afterwards. The venous pressure likewise showed no effect when the animal breathed under 4 cm. positive pressure, but a slight elevation at times took place when the animal was exposed to a pressure of 6 cm. of water. The rise in venous pressure was generally no
greater than 8 mm. of water, and, after injection of adrenalin, this rise sometimes did not take place.

The marked rise in systolic arterial pressure, following intravenous injection of adrenalin, was the only noteworthy finding in these experiments. It is of interest that application of positive pressure respiration either by intermittent inflation of the lung, by continuous pressure during inspiration

and expiration, or by a combination of both methods did not consistently modify the arterial pressure. It should be borne in mind, however, that the dose of adrenalin administered was an exceedingly large one for an animal of this size and that the vaso-constriction produced in the systemic arterial system was probably maximal. It was also surprising that the venous pressure was so little altered, even by respiration under 6 cm. of water pressure. We are unable to account for this except on the basis of an increased volume output of blood into the lungs on the part of the dilated right ventricle and a consequent increased diastolic filling of the right heart.

We may now attempt to interpret the pathogenesis of acute pulmonary edema produced in the rabbit by intravenous injection of adrenalin. Our results confirm those of Auer and Gates 8 and of Johnson 9 insofar as they
observed dilatation of the right ventricle and right auricle and a contracted state of the left ventricle. There seems to be no doubt that the left ventricle is in a condition of greater tone and smaller volume than the right and that its output of blood per unit of time is less than that of the right ventricle. The left auricle is moderately dilated. We may, therefore, assume that there is less diastolic filling of the left ventricle, its increased tonus being related to the markedly elevated systemic arterial pressure. It was also frequently observed that the right side of the heart contracted periodically, when all movement of the left ventricle had ceased, in animals autopsied three to five minutes after injection of adrenalin.

We were, however, unable to confirm the assumption of Auer and Gates and of Loeb that a pathologically elevated negative pressure was responsible for the occurrence of pulmonary edema. Our measurements showed a smaller range of intrapleural pressure, with the mean point between the inspiratory and expiratory intrapleural pressure approximately the same as that present before injection of adrenalin. We believe, therefore, that Welch's fundamental postulate of the cause of pulmonary edema applies to the condition that obtains in rabbits after intravenous injection of adrenalin, namely that there is an inequality in the output of the two ventricles, the right ventricle discharging an increased volume of blood into the lungs, the left ventricle emptying a smaller volume of blood into the systemic arterial system. The fact that the venous pressure is so little elevated under these circumstances confirms the interpretation that the right ventricle is emptying all the blood supplied to it.

In the presence of an increased discharge of blood from the right ventricle and a decreased output from the left, blood accumulates in the capillaries of the lung under increased pressure. This causes the diapedesis of red blood cells which may be observed within one minute after injection of adrenalin. In one-half to one minute later, a serous exudate filters through the capillary wall into the alveolar spaces. Our evidence suggests, to our mind, that the high capillary blood pressure is the significant factor in the pathogenesis of pulmonary edema due to adrenalin. It would seem likely that acute pulmonary edema when it occurs in human subjects as a result of left ventricular failure can be explained by a mechanism similar to the one which we have outlined.

The explanation of the therapeutic effect of positive pressure respiration appears to be more complicated. Although it has been shown in the roentgen-ray studies reported in this paper that dilatation of the right heart could be prevented, as well as pulmonary congestion and edema, by positive pressure respiration, we are not able to conclude that a decreased entrance of blood into the right heart is the sole or even most important factor. Edema of the lungs may be prevented by a degree of positive pressure which only slightly decreases the size of the heart. Furthermore, the application of even moderate positive pressure decreases significantly the mean intrapleural negative pressure. During continuous positive pressure respiration
the intrapleural pressure at the end of expiration is slightly above that of the atmosphere; during intermittent inflation of the lung, the intrapleural pressure during the inspiratory (or distending) cycle of respiration is also slightly above that of the atmosphere. We are, therefore, forced to conclude that the increase in positive pressure within the chest exerts an opposing force tending to hinder the outpouring of both red corpuscles and serum from the pulmonary capillaries. Although anoxemia is undoubtedly present as a result of the extreme shallowness of respiration, and although this is known to increase capillary permeability, the swiftness of development of the condition and the rapidity with which it may be stopped argues against anoxemia as a major influence.

Our experiments therefore lead to the conclusion that both the factors which we have just discussed operate to prevent or stop pulmonary edema. (1) A diminished volume of blood entering the right heart and hence the lung, due to the increased positive pressure within the chest. This in itself would result in a lower capillary blood pressure and, therefore, a decreased tendency for red corpuscles and serum to pass through the capillary wall. It may also be true that an intermittent application of positive pressure might squeeze some additional blood into the left auricle and into the ventricle, with an increased output of blood into the systemic arterial system. Since our studies showed no elevation of systolic arterial pressure under these conditions, we have no evidence to support this hypothesis. (2) The increased positive pressure shown to exist within the chest as a result of positive pressure respiration exerts an opposing force against the capillary wall which physically retards the outward filtration of red cells and serum. (3) Anoxemia is an additional although probably less important factor which increases capillary permeability. Distention of the pulmonary capillaries may also play a part in augmenting capillary permeability.

3. Physiological Measurement of the Effect of Positive Pressure on Human Subjects

The physiological effects of positive pressure respiration were studied in normal subjects, patients with congestive heart failure, and in a miscellaneous group. The measurements chosen were the pulse rate, respiratory rate, blood pressure, venous pressure, circulation time and vital capacity. The pressure varied from 3 to 8 cm. of water, administered continuously by means of a rebreathing apparatus consisting of a motor blower unit, a control valve inserted in the respiratory tubing, a water manometer and a soda lime container. The patient was connected to the apparatus by means of a mouthpiece, a mask or a hood with closure at the neck. This has been described elsewhere in detail in connection with helium-oxygen treatment. In some cases a basal metabolism apparatus was used with a weight on the bell to give the required pressure.
DATA ON NORMAL SUBJECTS

Ten normal subjects were tested. They breathed oxygen for a control period of five minutes under atmospheric pressure, oxygen under 3 cm. water pressure for five minutes, oxygen under 6 cm. water pressure for five minutes and oxygen under atmospheric pressure as the final control period.

The pulse rate in two of the ten cases showed no change when breathing oxygen under 6 cm. pressure. In eight cases, there was a decrease in rate, averaging 7 beats per minute. The respiratory rate was slightly increased in two subjects, decreased in three, with no change occurring in the remaining five. No significance can be attached to variations in respiratory rate in these tests. The systolic and diastolic arterial pressure also showed no appreciable alteration in the ten tested subjects.

However, the effect of positive pressure on the venous pressure was to cause a consistent slight elevation in the majority of instances; thus in eight of the ten individuals breathing against 3 cm. of pressure there was an average rise of 10 millimeters of water and in nine subjects breathing against 6 cm. of pressure there was an average rise of 20 mm. of water (table 1).

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<tr>
<td>5</td>
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<tr>
<td>10</td>
<td>93</td>
<td>101</td>
<td>107</td>
<td>92</td>
</tr>
</tbody>
</table>

The interpretation of this finding appears to be that the increased pressure within the chest produces a resistance to the entrance of blood in the right heart, thus creating a measurable elevation of the pressure in the systemic venous system. This explanation is further confirmed by the results on the circulation time, which show in the majority of instances a slight although definite prolongation. Thus, in five of nine subjects there was an average prolongation of circulation time of 3.3 seconds when the subjects breathed against 3 cm. of water pressure, and in six out of nine subjects a prolongation of 3.6 seconds when the subjects breathed against 6 cm. of water pressure (table 2). The effect of positive pressure, therefore, appears to be a slowing of the velocity of blood flow through the lung (arm to tongue time). From the results on the circulation time and the venous pressure it seems likely that the heart deals with a smaller volume of blood under these circumstances, presumably with a slower total blood flow.
TABLE II
Effect of Positive Pressure Respiration on Circulation Time in Normal Subjects

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Oxygen Under 0 cm. Pressure</th>
<th>Oxygen Under 3 cm. Pressure</th>
<th>Oxygen Under 6 cm. Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>26.0*</td>
<td>9.0*</td>
<td>23.0*</td>
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<td>2</td>
<td>19.0</td>
<td>17.8</td>
<td>16.7</td>
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<td>3</td>
<td>22.6</td>
<td>26.0</td>
<td>22.8</td>
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<tr>
<td>4</td>
<td>16.4</td>
<td>19.0</td>
<td>20.0</td>
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<td>20.4</td>
<td>19.8</td>
<td>21.2</td>
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</tr>
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<td>18.2</td>
<td>21.4</td>
<td>22.6</td>
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<td>19.2</td>
<td>22.6</td>
<td>23.8</td>
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<tr>
<td>9</td>
<td>16.2</td>
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</tr>
<tr>
<td>10</td>
<td>16.0</td>
<td>13.8</td>
<td>17.6</td>
</tr>
</tbody>
</table>

* Taken with saccharin (excluded); other tests done with sodium decholin.

The vital capacity in nine out of ten subjects showed an average decrease of 350 c.c., which may perhaps be accounted for by the fact that there is already an increase in the volume of air in the lungs as the result of positive pressure of approximately 300 to 400 c.c. when the vital capacity determination is made. In the accompanying graphic record of the effect of positive pressure respiration on the volume of gas in the lung (chart 7), it will be observed that a normal individual at the onset of pressure took into his lungs an additional 420 c.c. of oxygen; when the pressure was released, this additional volume of gas left the lung.

Chart 7. Effect of positive pressure respiration on the volume of gas in the lungs.
Effects of Positive Pressure Respiration in Patients with Congestive Heart Failure

Fourteen patients with congestive heart failure were tested as to their response under positive pressure. The degree of passive systemic venous congestion (i.e. congestive failure) may be seen from the control venous pressure measurements. The patients were divided into two groups of seven each.* In the first, control observations were taken while the patient was breathing air and oxygen for 5 minute periods at atmospheric pressure. The patients were then switched to breathing oxygen at 8 cm. water pressure for an 8 minute period and observations taken at the end of this time. Additional observations were recorded 3 minutes after pressure was withdrawn, while the patient was breathing air. In the second group, the patients breathed air during the control period, air during the administration of positive pressure (which in this group was 6 cm. of water) and 3 minutes after pressure was withdrawn. The results may be summarized as follows:

The pulse rate during positive pressure breathing was increased in six cases, averaging 6 beats per minute; decreased in one case, and no change in one case. In the group exposed to 6 cm. positive pressure, the pulse rate was increased in two cases, decreased in three, and no change in two cases. No significance could be ascribed to these changes, psychic influences and perhaps fatigue in all probability overshadowing the physiological influence of positive pressure. The same interpretation can be ascribed to the results on blood pressure in both groups. Excluding changes under 8 mm. Hg there were only three instances in both groups in which a marked change was observed. In these cases the systolic blood pressure rose 52 mm. in one case, 30 mm. in the second, and 25 mm. in the third. The diastolic blood pressure rose 38 mm. in the first case, 11 mm. in the second case and 18 mm. in the third case. In the remaining 12 cases the variations were negligible.

The respiratory rate in the first group was decreased in five cases an average of 3 breaths a minute, and increased in two, an average of 8 breaths per minute. In the second group exposed to 6 cm. positive pressure the respiratory rate was decreased in all, averaging 9 breaths per minute. The characteristic response to the inhalation under positive pressure is a decrease in the rate of respiration, although it did not occur in all of our cases.

As in the controls, the most consistent changes were in the venous pressures. In the group exposed to 8 cm. positive pressure, there was an elevation of venous pressure in seven instances, averaging 43 mm. of water, with a decrease in only one. In the group exposed to 6 cm. water pressure, there was an elevation of venous pressure in six instances, averaging 28 mm. of water, with a decrease in one (table 3). The degree of elevation of venous pressure in the patients with congestive heart failure was greater than in the control subjects who averaged an increase of 20 mm. of water when exposed to 6 cm. of pressure.

*In the first group of seven patients a repeat observation is made on one case, no. 4, so that the data will be presented as if there were eight cases instead of seven.
POSITIVE PRESSURE RESPIRATION

TABLE III

Effect of Positive Pressure Respiration on Venous Pressure in Patients with Congestive Heart Failure

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Before Application of Pressure</th>
<th>After Application of Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breathing Air</td>
<td>Breathing Oxygen</td>
</tr>
<tr>
<td>1</td>
<td>206</td>
<td>184</td>
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<td>3</td>
<td>65</td>
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<td>4</td>
<td>15</td>
<td>15</td>
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<tr>
<td>4A</td>
<td>5</td>
<td>-8</td>
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<tr>
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<td>105</td>
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<tr>
<td>16</td>
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<td></td>
</tr>
</tbody>
</table>

The effect of positive pressure on the circulation time was less consistent, perhaps due to the fact that many of these patients were too ill to furnish complete cooperation. Some of them had difficulty in keeping the mouth-piece in place during the entire period and the circulation time was taken within 3 minutes after pressure was withdrawn in these cases. The results may be summarized as follows: In the group exposed to 8 cm. positive pressure the circulation time while the patient was on the apparatus was unchanged in two. In two others it was markedly increased, one of them showing a prolongation of 16.5 seconds and the other 10.0 seconds. In the group exposed to 6 cm. positive pressure, observations were taken within 3 minutes after pressure was withdrawn. In two cases there was no change, but in three others there was a marked prolongation, averaging 17 seconds. Although lengthening of the circulation time did not occur in all instances, the change when it did take place was much more marked than in the control subjects in whom prolongation of the circulation time when breathing against 6 cm. positive pressure averaged only 3.6 seconds (table 4).

The vital capacity showed no consistent changes in the group breathing under 8 cm. positive pressure. However, in the group breathing under 6 cm. positive pressure, approximately 5 minutes after conclusion of the test, there was a rise in six out of seven patients, averaging 216 c.c. The fact that this rise in vital capacity did not occur in the group breathing under 8 cm. positive pressure may be accounted for perhaps by the greater fatigue induced in the latter group by a longer experiment. A possible explanation
for the elevation in vital capacity is that some blood was forced out of the lungs into the left heart during the test, allowing greater lung space, although this must be presented only as a tentative hypothesis.

**Table IV**

Effect of Positive Pressure Respiration on Circulation Time in Patients with Congestive Heart Failure

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Before Application of Pressure</th>
<th>After Application of Pressure</th>
<th>3 Minutes After Pressure Was Withdrawn Breathing Air</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breathing Air</td>
<td>Breathing Oxygen</td>
<td>Breathing Oxygen Under Pressure</td>
</tr>
<tr>
<td>1</td>
<td>43.6</td>
<td></td>
<td>61.5</td>
</tr>
<tr>
<td>2</td>
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<td>14.0</td>
</tr>
<tr>
<td>3</td>
<td>14.0</td>
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<td>38.2</td>
</tr>
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<td>4</td>
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<td>41.0</td>
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<tr>
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<td>39.0</td>
<td></td>
<td></td>
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<tr>
<td>13</td>
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</tr>
<tr>
<td>14</td>
<td>23.0</td>
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<td></td>
</tr>
</tbody>
</table>

We wish to present three charts showing the significant changes in typical experiments. In the chart below (chart 8) the effect of breathing against positive pressure is shown in a patient with congestive heart failure. It will be seen that the venous pressure declines during the control period from 205 to 182 mm., begins to rise after the application of 3 cm. positive pressure, shows a still more marked elevation at 6 cm. positive pressure, reaching 225 mm., and then falls abruptly when the pressure is removed. The circulation time rose from 43 seconds to 53 seconds.

In a patient with asthma (chart 9) the venous pressure rose only slightly with 3 cm. positive pressure, from 30 to 40 mm., but rose to a height of 75 mm. when 6 cm. positive pressure was used, falling to 25 mm. when pressure was withdrawn. No significant changes took place in blood pressure or pulse or respiratory rate in any of these cases.

The last chart represents a reaction in a patient with neurocirculatory asthenia (disordered action of the heart) to positive pressure respiration (chart 10). The patient, a young man of 22 years, came to the hospital complaining of breathlessness at rest, palpitation and continuous heart consciousness. He was extremely apprehensive. On examination, his heart showed no abnormalities, the electrocardiogram was normal and roentgen-ray of the heart revealed no enlargement. The test was performed with the
patient in a helmet, a leak-tight closure being made at the neck. Oxygen was breathed throughout. The chart shows that when he was breathing against 2 cm. positive pressure, there was a distinct rise in venous pressure on two occasions, from 90 to 120 mm. When the pressure was raised to 5 cm., the venous pressure rose still further to 138 mm. and dropped abruptly to 90 when the pressure was removed. The circulation time increased from 18 seconds to 27 seconds while he was breathing under 5 cm. water pressure.

This case is of considerable interest in that it portrays physiological changes in a patient whose circulatory symptoms are of nervous origin. In another patient who had anxiety neurosis but without symptoms referable to her heart, the same test showed no elevation of venous pressure when breathing against 2 cm. water pressure and no change in circulation time. It would seem likely, therefore, that the rise in venous pressure which occurs after breathing against positive pressure is an indication of an inability of the heart to compensate for an arbitrarily induced back pressure by an increased blood flow. In normal individuals a mechanism exists whereby
the circulation time is only slightly affected by resistance to the flow of blood into the heart, whereas in patients with heart disease, especially congestive failure, marked retardation of the velocity of blood flow may take place.

![Graph showing changes in venous pressure, systolic and diastolic blood pressure, pulse, respiratory rate, and circulation time over 60 minutes.]

**Chart 9.** Effect of breathing against positive pressure in a patient with asthma.

An explanation of the relatively marked increase in venous pressure and prolongation of circulation time in patients with congestive heart failure exposed to positive pressure respiration invites consideration of several influences. In the first place, the increase of positive pressure within the chest interposes an obvious difficulty to blood entering the right auricle. However, this physical difficulty would appear to be of similar magnitude, other factors being equal, in normal subjects who, however, show comparatively
slight changes. It has recently been shown by Christie and Meakins 27 that the patient with congestive heart failure has an intrapleural pressure range that is more nearly atmospheric than the normal individual, especially during expiration. The presence of so much additional blood in the lungs inter-

![Chart 10.](http://annals.org/)

feres with the elasticity of the pulmonary membrane with the result that the cardiac patient is unable to achieve as high a negative pressure during the inspiratory cycle as the normal person. The cardiac patient would therefore be less able to increase the negative pressure within the chest and so in part lessen the additional positive pressure imposed on the lung from without, whereas the normal individual by an increase in the velocity and depth of breathing could increase the negative pressure within the chest to a degree which would practically overcome the arbitrarily imposed external positive pressure. In this way an explanation is afforded of the relatively small increase in venous pressure and the relatively insignificant interference with the velocity of the circulation that normal individuals show. Some of the variability in our results in patients may also perhaps be explained in
this way, since an individual who because of psychic influences was hyper-ventilating at the time the circulation test was being made might be temporarily developing an increase in the negative intrapleural pressure which would augment the blood flow. As pointed out in the historical section of this paper, it has been repeatedly shown that an increase in the negative pressure within the chest increases the blood flow both through the lungs and the peripheral circulation.

An additional influence may be set forth, namely, that the presence of an increased positive pressure within the chest interferes with the diastolic filling of the ventricles and the auricles as well, and that this interference would be more apt to have an adverse influence in a diseased heart muscle than in a normal one. It also seems likely that the increased pressure within the lung may in the case of an insufficient right ventricle retard a complete emptying of that chamber of the heart, thus causing a further back pressure of blood into the systemic veins.

We have not discussed up to the present whether this repression of blood into the systemic venous reservoir is an adverse or a beneficial influence. At first sight it might seem that such a slowing of the circulation time would but increase the congestion of the viscera and extremities and thereby accentuate the harmful effects of heart failure. We must consider, however, that this effect is accomplished by decreasing the volume of blood passing through the heart. The heart is at this time dealing with a smaller blood volume which would decrease the burden upon it, and thus have a beneficial influence. One has only to remember the dramatic improvement in some cases with acute congestive heart failure particularly in left ventricular failure that is engineered by withdrawal of 500 c.c. of blood. Striking improvement in the circulation has also been reported by tourniquets applied to the lower extremities. In both instances, the heart muscle for a brief period of several hours is allowed to function on a smaller volume of blood and its recuperative power under these circumstances is at times startling. We feel justified in broaching the proposition that positive pressure respiration, properly controlled, may diminish the volume of blood the heart has to deal with and, therefore, constitute a beneficial rather than an adverse influence. Studies with this in mind are contemplated, namely, the effect of more continuous but somewhat milder degrees of positive pressure administered continuously during inspiration and expiration to patients with various forms of heart failure. We have outlined the discussion at this time, since it may account in part for some of the improvement observed in treating patients with pulmonary edema, to be described in the following section.

**The Clinical Use of Positive Pressure Respiration in Acute Pulmonary Edema**

The technic of applying positive pressure continuously throughout the respiratory cycle has been described in detail in connection with helium-
positive pressure respiration.\textsuperscript{26,20} The method consists of the provision of a closed circuit apparatus in which the ventilation and pressure are achieved by a motor blower unit capable of maintaining a pressure as high as 10 cm. of water. In the earlier cases, a mouthpiece or mask was used to connect the patient with the apparatus. Later a hood was employed which made closure at the neck, modelled after the Benedict helmet metabolism apparatus. We shall present eight case histories which illustrate the clinical use of this therapeutic procedure.

**Case Reports**

*Case 1.* A female, aged 54 years, had suffered from nervousness, weakness and heart pounding for four and a half years; on examination she was found to have a toxic adenoma. The basal metabolic rate was plus 27 per cent. The heart was moderately enlarged, blood pressure 200 systolic and 100 diastolic. The heart rate was 140. After iodine administration and rest in bed, she improved and thyroidectomy was performed. The day after operation she showed signs of advanced cardio-respiratory failure and became intensely dyspneic and cyanotic. Supra-ternal retraction was evident during inspiration. The pulse rate was rapid, 140, thready volume and soft. Blood pressure dropped to 80 systolic and 60 diastolic and returned to 120 systolic and 80 diastolic. The venous pressure climbed to 280 mm. Moist râles were heard throughout both lungs and audible gurgling appeared in her throat. Her head moved backward with each inspiration. Respiration was extremely shallow and rapid, rate 50. She appeared moribund.

She was treated with inhalation of 50 per cent helium and 50 per cent oxygen under a pressure of 7 cm. of water, lowered later to 5 cm. Within 15 minutes, the signs of pulmonary edema had disappeared. There were no gurgling noises, the moist râles were no longer audible. Improvement continued. She became conscious and five hours later breathing was deep and easy, the lungs were clear, cyanosis was greatly lessened. The pulse was of good volume, rate 120, blood pressure 160 systolic and 120 diastolic. Venous pressure was 125 mm.

The patient's temperature, however, continued to rise. When the mouthpiece rebreathing apparatus was removed for one minute, the signs of edema began to reappear. During the night she showed returning circulatory failure, pulse rate 160, venous pressure 250 mm., blood pressure 190 systolic and 100 diastolic, dropping later to 130/. Temperature was 107\textdegree F. She died the following morning. Before death, no râles could be heard over the front of her chest.

A thyroid crisis associated with circulatory failure was the apparent cause of death. The earlier clinical improvement as a result of the application of positive pressure was striking. Helium was added to oxygen because the marked supra-ternal retraction suggested some degree of obstruction of the respiratory passages. The rapid disappearance of edema was distinctly due to the administration of pressure, as it recurred almost immediately after withdrawal of positive pressure. The cause of edema seemed to be mainly the result of left ventricular failure.

*Case 2.* A male, aged 50 years, developed acute bronchopneumonia following hemorrhage from a tuberculous lesion. On the fourth day, acute pulmonary edema, together with signs of cardiac failure, was manifest. The pulse became rapid, 150, thin and thready, and the liver was palpable two fingers below the costal margin. A mixture of 50 per cent helium and 50 per cent oxygen was given under 5 cm. pressure. Physical examination of his chest one hour later revealed absence of all moisture in the lungs. Twelve hours later, the pulse was 100, respiratory rate was 24, and he was comfortable. The rebreathing pressure apparatus was removed without recurrence of edema. However, the patient's temperature rose abruptly with
a spread of the bronchopneumonic process, but without pulmonary edema. He died 24 hours later.

The cause of pulmonary edema was thought to be due to the joint influence of left ventricular failure and increase in capillary permeability associated with inflammation of the lung and anoxemia.

Case 3. Male, aged 62 years. History: The patient’s mother had asthma and he himself suffered from hay fever for six years. Asthma began three years before admission, relieved by adrenalin. Patient entered the hospital in a state of severe status asthmaticus unrelieved by three injections of adrenalin, 1 c.c. each, and an injection of morphine, gr. ¾ during a five hour period. He was in a generalized spastic state with marked carpopedal spasm. Inspiratory dyspnea was extremely severe and the patient suddenly stopped breathing. After injection of 1 c.c. of adrenalin he began breathing again but with extreme difficulty. The respiratory rate decreased progressively to two per minute. Blood pressure dropped from 170 systolic and 110 diastolic to 110 systolic and 70 diastolic. He developed edema of the lungs and frothy fluid came into his mouth. He was pale, eyes were rolled back and his jaws clamped. The pupils did not react to light. Inspiration was short, respiration prolonged with a high-pitched sibilant whistle. The pulse was at first fast and irregular and later imperceptible. Fifty c.c. of 50 per cent glucose intravenously had been administered without noticeable effect. He was then put in the hood helium apparatus with 21 per cent oxygen and 79 per cent helium and 5 cm. water pressure. Breathing increased in depth and rate and the pulse became palpable. He was given 10 c.c. of calcium gluconate and 20 c.c. of dilute hydrochloric acid (1–1,000) intravenously without effect on the marked spasm. Metrazol was injected subcutaneously in 4 c.c. doses at two hour intervals for three doses. The breathing progressively improved and 12 hours later he was out of danger with slight asthma persisting. The signs of edema disappeared within the first hour of the treatment. On the following day helium was discontinued and the day after the patient was free from asthma. He left the hospital without asthma, one week later.

In this patient edema of the lungs appeared to develop as a result of:

1. A previously existing pathologically elevated negative pressure due to inspiratory dyspnea, which exerted a suction action on the pulmonary capillaries.
2. Fatigue and imminent paralysis of the respiratory center. (To be discussed in case 7.)
3. Left ventricular failure.

The rapid pulse with marked decrease in volume which patients with asthma develop appears to be due to the high negative pressure existing within the chest which facilitates the entrance of blood into the right side of the heart and into the lungs but retards the passage of blood from the chest into the aorta. It may be generally observed that the volume of the pulse is either markedly diminished or becomes imperceptible at the end of the inspiratory cycle when the negative pressure within the chest is at its height. During expiration the pulse returns and increases in volume. The blood pressure frequently drops below the point of determination at the end of inspiration. It seems, therefore, likely that in this patient passive pulmonary congestion was present due to the failure of the left ventricle to discharge the customary volume of blood.

Case 4. A female, aged 37 years, became acutely ill two days after onset of a coryza, with the development two days later of signs of consolidation in the right upper lobe. She showed progressive pulmonary involvement, with high fever and marked toxicity. All lobes showed consolidation except the left lower lobe. The sputum and blood contained pneumococcus type V. Treatment with positive pressure, 5 to 7 cm. water, and 100 per cent oxygen was applied when exitus seemed
momentarily imminent. She was comatose and deeply cyanotic. Respiration was very labored with moist râles heard extensively over the anterior portion of the chest and in the throat. Retraction was present in the supraclavicular fossa. Pulse was very thin, rate 150. Blood pressure had dropped from 160 systolic and 85 diastolic to 110 systolic and 50 diastolic.

Within 15 minutes after initiation of positive pressure, all signs of edema cleared. She breathed more deeply, with less supra-ternal retraction and labor. Cyanosis was markedly diminished and pulse rate and volume improved. No decline in fever or toxicity occurred, and she died 48 hours later, temperature 106.2°. The signs of edema continued to be absent as long as positive pressure was maintained, but returned when the apparatus was removed. The cause of the pulmonary edema was thought to be increased capillary permeability due to inflammation and anoxemia, with left ventricular failure as a contributory cause.

Case 5. A male, 72 years, showed a rising temperature the day after a second stage supra-pubic prostatectomy. On the fourth day his temperature was 104.6°, pulse 120, thin and soft, respirations 40. He became comatose, moist râles appeared throughout the lungs, and he appeared moribund. The clinical diagnosis was bronchopneumonia, edema of the lungs, cardiac insufficiency. He was treated with 100 per cent oxygen under a pressure of 5 cm. of water, using a mouthpiece rebreathing apparatus. The signs of edema were markedly decreased within 15 minutes, the pulse rate decreased from 120 to 108, his breathing was deeper, and moderate cyanosis previously present was much lessened. His lungs did not again show outspoken edema. However, his pulse weakened and on the following morning, 20 hours after the onset of positive pressure, he died, death being due to cardiac failure. The cause of pulmonary edema was thought to be left ventricular failure with an increased capillary permeability due to pneumonia.

Case 6. Female, aged 26 years. History: The patient had pneumonia two months previously. She now entered the hospital with fever, dyspnea and a pain in her chest for four days. A rising temperature and pulse continued for three days and she appeared extremely ill with severe dyspnea accompanied by neck muscle retraction on inspiration and a moderate degree of cyanosis in an oxygen tent with 50 per cent oxygen concentration. The respiratory rate was 40. Examination of the lungs revealed fine crackling (crepitant) râles over the right upper lung and the left upper lung and left axilla, with many moist râles over the anterior and axillary regions on the left side. Over the heart presystolic and systolic murmurs were heard at the apex. The pulse was 120 and small in volume. White blood cells 20,600, polymorphonuclears 86 per cent. Sputum culture revealed Friedländer's bacillus.

The patient was treated with 100 per cent oxygen under a positive pressure of 3 cm. of water. After 15 minutes there appeared to be a definite although not marked diminution in the number of moist râles over the left anterior chest. However, there was no change in the number or character of the fine sticky râles. One hour later there seemed to be a slight further lessening of the number of moist râles. On the following day the patient was improved. There was a smaller number of both fine and medium moist râles over the chest. She was treated for one hour with 100 per cent oxygen under a positive pressure varying from 3 to 5 cm. of water. There was no definite change in the râles in the chest. The patient appeared completely comfortable in the hood on both occasions. The dyspnea was less marked and there was a distinct lessening of the retraction of the neck muscles during inspiration.

No consistent changes were observed in either the systolic or diastolic blood pressure, the pulse and respiratory rates. No change in the venous pressure could be attributed to breathing against 3 cm. positive pressure but when 5 cm. was employed there was a consistent but very slight increase of the venous pressure, ap-
proximately 10 mm. of water. This degree of elevation of the venous pressure is extremely little when compared to the effect of positive respiration on patients with congestive heart failure, and indicates that the patient was able to compensate in some way for the resistance interposed to the flow of blood into the right heart. In fact, normal subjects generally showed a rise of 20 mm. of water; this may be due to the increased blood flow associated with the pneumonia.

The patient gradually improved and recovered. The case is presented primarily to indicate that positive pressure respiration of the degree employed does not result in a disappearance of râles which are presumably of an inflammatory etiology. There was no change in the fine sticky râles although there was a slight but definite diminution of the larger moist râles over the front of the left chest. The function of positive pressure in causing a more marked relief of dyspnea was clearly revealed. The inspiratory neck muscle retraction gave evidence that the widely consolidated lung was moved only by a markedly increased inspiratory effort. This was plainly alleviated by the inhalation of oxygen under positive pressure. It was also of interest that no significant changes occurred in the circulation except the extremely slight elevation in venous pressure noted above. Although the large and medium-sized moist râles appeared to indicate the beginning of pulmonary edema it is impossible to state that the short period of treatment given the patient had anything to do with the outcome. The case is presented not as a therapeutic result but to indicate the limitations of positive pressure respiration in checking or in removing inflammatory exudate, in the same time interval in which a transudate of edema fluid can be abolished. It is not possible to say what a longer period of treatment would have accomplished but it is of interest that the patient was more comfortable under positive pressure respiration than she was in atmospheric oxygen.

Case 7. Male, aged 59 years. History: Following an attack of bronchopneumonia, which seemed to clear, the patient developed asthmatic breathing, a harassing cough, and mucopurulent expectoration. The asthmatic breathing, though varying in intensity, became progressively worse in the succeeding two months, and was unrelieved by adrenalin, rest in bed, or oxygen. There were apparently no contributory factors in the past history. He was removed to the hospital in acute distress, breathing with severe difficulty, with markedly prolonged expiration. Sibilant râles were heard throughout the chest. Moderate relief was obtained by two treatments of helium and oxygen under 4 cm. positive pressure. He was put into an oxygen tent, oxygen concentration 50 per cent, for the night with the idea of resuming helium therapy in the morning. Three doses of morphine, grains ³⁄₄ each, were given during the night, the last administered without the knowledge of the attending physician. When he was seen in the morning his condition appeared moribund. He was a large well-developed man, cyanotic even in 50 per cent oxygen. Respiratory rate had declined to 2 to 4 times a minute. The breathing took place as a short gasp, accompanied by a loud mucous gurgling which emanated from his throat and partially obscured the moist and sibilant râles heard on auscultation over the front of the chest. His pulse was full and bounding, rate 90, apparently an asphyxial pulse. He had been given 50 c.c. of 50 per cent glucose intravenously without noticeable relief. In the presence of what appeared to be imminent asphyxia due to respiratory failure he was given 21 per cent oxygen and 79 per cent helium under 5 cm. positive pressure, at first through a mouthpiece and later through a mask closed-circuit apparatus. Within 10 minutes signs of pulmonary edema had cleared and auscultation of the chest showed that both lungs were being ventilated, accompanied by sibilant râles in inspiration and expiration. The respiratory rate had increased to 16. He was given 4 c.c. of metrazol and 20 grains of caffeine sodium benzoate in divided doses during the first half hour. The patient progressively improved and in an hour and a half opened his eyes and was partly conscious. His pulse was rapid, rate 136, but of
fair quality. He was kept on the helium-oxygen mixture for three days, the pressure being gradually lowered from 5 to 2 cm. of water. At the end of that time the patient was in generally good condition. Although a moderate amount of asthmatic breathing continued, his pulse declined to 86 and he was eating three good meals a day.

On two subsequent occasions the patient developed severe obstructive dyspnea which required helium treatment for a period of a week almost continuously, with intermittent inhalations of helium with oxygen at intervals following the continuous treatment. He was treated with autogenous and stock vaccines, potassium iodide and roentgen-ray therapy. Two bronchoscopies were performed which revealed unusually small bronchi, their diameter comparable to that expected in an older child. After a series of reversals the patient seemed on the road to recovery, although at no time was his chest free from sibilant râles. For a period of one month, however, he seemed in such good condition as to be allowed up in a chair and to do a small amount of walking. A graphic record of his tidal air showed expiration to occupy 69.9 per cent of the respiratory cycle, whereas three months before it was 86.7 per cent. It is noteworthy that at no time did injection of adrenalin clear the râles in his chest, although improvement was often noted following its use, and some improvement following the inhalation of a 1–100 adrenalin spray. The patient had planned to leave the hospital in one week, when a return of severe difficult breathing took place, apparently associated with increased activity. His condition became progressively worse, and finally gasping respiration necessitated the use of helium and oxygen with a positive pressure of 5 cm. of water. This gave him a moderate degree of relief, and it was thought that the condition would yield to treatment as it had three times in the past. However, each time the hood was removed, the patient was plunged into severe uncontrollable obstructive dyspnea. The patient died one week later of respiratory failure.

The diagnosis of this patient was (1) obliterative bronchitis and bronchiolitis of infectious origin, (2) edema of the lungs (the morning after admission to the hospital).

There was evidently not only an unusual narrowing of the main bronchi, but also a progressive intimal thickening of the bronchioles as well. The patient was in the hospital six months. It was believed that in the next to the last week of illness helium-oxygen therapy was postponed for a period sufficient to cause a marked increase in edema of the walls of the smaller bronchi and bronchioles due to the persisting pathologically elevated negative pressure within the chest.

The patient's reaction to helium-oxygen treatment under 5 cm. water pressure the morning after admission could be attributed mainly to the maintenance of the positive pressure, which appeared to result in a swift disappearance of pulmonary edema, the restoration of pulmonary reflexes and return of activity of the respiratory center. The function of helium was undoubtedly to allow a deeper penetration of the mixture of 21 per cent oxygen and 79 per cent helium, but this could not have been achieved unless the edema had first cleared.

The cause of the initial pulmonary edema was considered due to (1) the previous presence of a high intrathoracic negative pressure resulting from inspiratory dyspnea, (2) the administration of excessive doses of morphine. By depressing the respiratory center, the respiratory rate was not only markedly decreased but there was a diminution in expiratory effort. The patient with asthma, by maintaining a prolonged expiration against a constricted orifice, develops an increased positive pressure between the site of obstruction and the alveolar capillaries. The abrupt termination of this pressure, by decreasing the intensity and rate of respiration, is followed by an increase in permeability of the capillary wall, as will be more fully discussed later.

Case 8. Male, aged 50 years. History: Patient entered hospital complaining of
epigastric distress, an aching pain in the lower left chest of six months' duration. He had a productive cough with blood streaked sputum and during this period lost 22 pounds. When he was admitted to the hospital, examination of the chest showed bronchial breathing and dullness over the left lower lobe. The brachial arteries were palpable, blood pressure was 130 systolic and 75 diastolic. As a result of bronchoscopy and biopsy, a diagnosis of carcinoma of the left bronchus with involvement of the lung, atelectasis and pleural effusion was made. Following a finger infection, for which he was given prontylin, he developed bronchopneumonia on the ward with widespread consolidation, and, two days later, edema of the lungs. He became deeply cyanotic, a loud gurgling was heard in his throat and moist râles over the chest. His pulse was 136 and of small volume, respiratory rate 40, temperature 103°. The administration of 50 per cent oxygen in an oxygen tent only slightly relieved the marked cyanosis. Positive pressure respiration was used with 100 per cent oxygen under 6 cm. water pressure and within one hour the patient was much improved, there was no gurgling to be heard in the throat and many but not all of the moist râles had cleared. His color was markedly improved. A roentgen-ray of the chest showed a tremendous amount of irregular consolidation and metastases as well as marked cardiac enlargement. One hour after positive pressure respiration, a repeat roentgen-ray of the chest at the same distance showed the heart shadow was decreased 1.5 cm. in its transverse diameter, and a marked increase had occurred in the radiability of both lung fields. The breathing continued to be shallow and the patient failed to make a further improvement. Twenty-one hours later respiration became slower and more shallow and the patient died of respiratory failure. A few moist râles were still heard over the chest but there was no recurrence of the widespread edema present before treatment. The cause of edema in his case seemed more closely related to the factor of increased permeability due to inflammation and anoxemia, perhaps accentuated by prontylin. Left ventricular failure may have been a secondary contributory factor.

**DISCUSSION**

The cases that have just been reviewed indicate that positive pressure respiration may be used as an effective therapeutic procedure in acute edema of the lungs. The primary illness in which pulmonary edema occurs as a complication is frequently of such severity that an ultimate recovery cannot always be expected. However, there are cases as moribund as occurred in this series in which a clearance of pulmonary edema allows the patient opportunity to recover from the primary illness.

The pathogenesis of acute edema of the lungs is a varied one. The factors involved may be listed as follows: 1. Left ventricular failure. 2. Increased permeability of the pulmonary capillaries. 3. (a) A persisting pathologically elevated negative pressure within the chest, or (b) an abrupt termination of expiratory effort and a consequent loss of the backward pressure on the pulmonary capillaries. In case 1 the essential factor appeared to be left ventricular failure. Right ventricular failure was also present. Following removal of the thyroid gland the patient developed a thyroid crisis which was the exciting cause of cardiac failure the day after operation. The pulse became extremely rapid and in small volume. The blood pressure dropped to as low as 80 systolic and 60 diastolic, the venous pressure climbed to 280 mm. of water. Moist râles appeared in both lungs and gurgling was heard from the throat. It would seem likely that failure
of the left ventricle was responsible for backing up of blood in the lungs, increased hydrostatic pressure outward from the distended capillaries and finally exudation of serum. Since some anoxemia and capillary distention were also present, an additional factor may have been increased permeability of the lung. The marked elevation in venous pressure indicated an associated failure of the right ventricle. The swift clearance of pulmonary edema following the administration of a pressure of 7 cm. of water exerted a direct opposing force on the pulmonary capillaries, counteracting their tendency to ooze serum. The effect of positive pressure within the chest was also to retard the entrance of blood into the right heart and relieve the left ventricle as well as the right. As a result breathing became deep and easy, the lungs were clear and the circulation markedly improved. The venous pressure fell to 125 mm. In this instance, there was for a temporary period not only a clearance of pulmonary edema but a restoration of some degree of function of both the left and right ventricle.

In case 5 a man 72 years old on the fourth day following a prostatectomy developed broncho-pneumonia associated with cardiac insufficiency and edema of the lungs. In this case there were probably two factors at work, left ventricular failure and an increased capillary permeability due to pneumonic inflammation, anoxemia and capillary distention.

Case 4 was a woman of 37 years of age who suffered from massive consolidation of both lungs due to pneumococcus type 5. There was a blood stream infection with the same organism. Development of edema in her case seemed to be associated with increased capillary permeability due to inflammation and anoxemia. The fact that the pulse volume was extremely small with a rate of 150 and that the blood pressure dropped from 160 systolic and 85 diastolic to 110 systolic and 50 diastolic suggested that left ventricular failure was a contributory cause.

In case 2 a man of 50 years developed acute broncho-pneumonia following a hemorrhage from tuberculous lesion. On the fourth day, acute pulmonary edema developed accompanied by the signs of heart failure. The pulse mounted to 150 and was of small volume. The liver was palpable two fingers below the costal margin. In this case, left ventricular failure appeared to be the precipitating cause with increased permeability, due to inflammation and anoxemia, as the contributing factor. The clearance of pulmonary edema, the fall in pulse rate to 100 and the disappearance of other signs of cardiac failure, which took place in this patient, indicated that positive pressure respiration exerted its effect both as a physical force opposing a further tendency of the capillaries to ooze serum and as a restoration of cardiac function by limiting the volume of blood handled by the heart. The fact that 12 hours later pressure could be removed without recurrence of edema was added evidence that the essential cause of the edema was left ventricular failure.

The cases that have just been reviewed have some similarity to the experimental production of pulmonary edema following intravenous injec-
tion of adrenalin. In this type of edema our experimental evidence suggests that retarding the flow of blood into the right heart, thus enabling the heart to deal with a smaller volume, is of value in helping it to regain its function. The action of positive pressure in this respect is comparable to tourniqueting the extremities which is a therapeutic procedure of value in pulmonary edema.

In case 8, a man with widespread carcinoma of the lungs who developed broncho-pneumonia, the onset of edema of the lungs appeared to be associated with an increased permeability of the pulmonary capillaries as the most likely essential factor, with left ventricular failure as a contributing cause. One hour after positive pressure respiration was begun roentgen-rays showed a marked increase in radiability of both lung fields and a decrease in the transverse diameter of the heart of 1.5 cm. In his case not all of the moist râles in the lungs disappeared but the clinical improvement was at first quite marked. In case 6, a young woman with pneumonia due to the Friedländer bacillus, positive respiration was followed by a diminution of the loud moist râles over the anterior chest but not by any change in the crepitating râles. In another patient (whose case history is not reported in this paper), a clinical diagnosis of acute pulmonary edema following broncho-pneumonia was not confirmed by autopsy. A woman of 54 years of age was ill for seven days with fever, cough and dyspnea. On physical examination, scattered moist râles were present over both chests from the onset of illness. She had long-standing mitral valvular disease with enlarged heart. On the seventh day of disease, severe dyspnea developed, accompanied by loud moist râles over the anterior chest and gurgling noises emanating from the throat. After three hours of positive respiration, 6.0 cm. positive pressure being employed in the hood, the right anterior chest was free from râles during inspiration, although loud moist râles could still be heard over the left anterior chest. There was an initial clinical improvement during the first eight hours of treatment which was followed by a progressive weakening of the patient and death 12 hours later. At autopsy, no pulmonary edema was found; the bronchi were filled with purulent exudate. The moist râles evidently had their origin in the bronchi and were apparently due to inflammatory exudate and not a serous transudation. Although the inspiratory dyspnea was relieved by distention of the lungs from without, there was only a partial clearing of the widespread signs of moisture.

The effectiveness of positive respiration seems more pronounced in the cases in which serous oozing is present and less noticeable in those in which inflammatory exudate is the cause of the râles in the chest. In the majority of cases of pneumonia, the onset of pulmonary edema is not accompanied by a prolonged circulation time, according to King and his collaborators, which would suggest that pulmonary congestion due to heart failure is not the precipitating cause of the condition. However, more cases of pulmonary edema in pneumonia will have to be studied before the value of this treat-
ment can be determined. The most convincing and dramatic response to positive pressure respiration has occurred in those patients in whom some degree of failure of the left heart seemed clinically evident. In cases 3 and 7, the cause of pulmonary edema appeared to be different from that in the group just discussed. A predisposing factor seemed to be the previous presence of a high negative pressure within the chest due to severe inspiratory dyspnea, which may be compared to the development of pulmonary edema in animals subjected to respiration against a narrow orifice or against negative pressure.

In the discussion on the experimental production of edema that occurred after tracheal stenosis it was shown that the intrapleural negative pressure might increase to 10 times the normal value and that the heightened negative pressure exerted a suction action on the pulmonary capillaries. The same influence aided the inflow of blood into the right heart and hindered the exit of blood from the chest into the extra-thoracic aorta; thus, the factor of pulmonary congestion was added. In severe asthma the same mechanical influence takes place. The senior author has on one occasion demonstrated a markedly elevated negative pressure (—17 cm. of water) in a case of severe asthma.

There is another important factor in the development of pulmonary edema in the two cases now being discussed. In each of them it will be remembered that the respiration rate decreased to two per minute. In case 7, three doses of morphine were given during the night. By depressing the respiratory center, the respiratory rate was not only markedly decreased but there was a marked diminution in the force of respiration. The ventilation of the lungs was, therefore, markedly diminished with the result that severe anoxemia was present, which is itself a factor in increasing capillary permeability. There is, however, still another factor that seems to be significant, namely, a sudden loss of a previously existing positive pressure against the pulmonary capillaries due to the patient’s own expiratory efforts. The prolonged expiration of the patient with asthma results in an increased positive pressure between the site of bronchial constriction and alveolar capillaries. When this high positive pressure is abruptly terminated, the pulmonary capillaries become immediately more permeable.

It has long been known that in patients in whom laryngeal obstruction has existed for a considerable period, the provision of an unrestricted airway by tracheotomy is regularly followed by an outpouring of edema fluid from the lungs and bronchi into the trachea, which requires aspiration and suction at half hour to one hour intervals for many days and sometimes weeks. Woodman showed that when the patient, immediately after tracheotomy, was made to exhale under a positive pressure comparable to that present prior to the relief of the obstruction that edema fluid would not collect in the trachea. Kernan and Barach treated three patients who began to show this characteristic filling of trachea and bronchi with edema fluid by the application of positive pressure during the expiratory cycle. The pres-
sure at the beginning of treatment was 7 cm. of water. This was gradually lowered during a two day period when the pressure was removed without any recurrence of edema fluid in the trachea. In one of these patients who had carcinoma of the lung there was the additional complication of hemorrhage. In this case after three hours of respiration against positive pressure there was not only an absence of edema fluid but the bleeding had stopped. This suggests that positive pressure may be used for cases of hemorrhage from the lung of capillary or venous origin.

There is, therefore, definite evidence that the sudden removal of a previously existing backward pressure on the pulmonary capillaries is followed by an increased permeability of the capillary wall and that the re-establishment of this positive pressure comparable to what the patient had become accustomed to stops the leakage of serum. In patients with asthma the use of morphine in doses which markedly diminish the respiratory effort has, therefore, the danger of precipitating edema of the lungs. The sudden development of pulmonary edema after aspiration of pleural effusion may be due at least in part to sudden removal of a relative positive pressure and exposure of certain lung alveoli to resumption of negative pressure.

The senior author has already suggested that the expiratory grunt in lobar pneumonia has the physiological advantage of maintaining increased positive pressure against the alveolar capillaries at the beginning of expiration. That this grunting respiration is not simply a subjective complaint on the part of the patient but has the functional significance of preventing pulmonary edema was suggested by the observation of a case of lobar pneumonia that developed acute edema of the lungs following the administration of ½ grain of morphine. The patient had extensive involvement of both lungs due to pneumococcus type 3. He was in marked dyspnea and emitted a loud grunt at the start of expiration. After the administration of morphine the patient's respiration became shallow and slow without any grunt. He went to sleep and one hour afterwards had generalized edema of the lungs.

It has also been pointed out that patients with emphysema frequently partially close their lips during expiration and find that their breathing is made easier than when the mouth is open. We have made use of this observation in the treatment of patients with chronic asthma of moderate degree suggesting to the patient that he arbitrarily increase the resistance to the egress of air during expiration. In many instances a therapeutic exercise of this character pursued for three to five minutes will terminate an attack of wheezing, indicating that this backward distending pressure on the bronchioles tends to keep them patent. Certain areas of the lungs may have become accessible to ventilation, which previously were shut off by collapsed ducts or thin webs of mucus.

We do not mean to condemn completely the use of morphine for asthma or pneumonia since a moderate decrease in pulmonary ventilation relieves inspiratory dyspnea and lowers the negative intrapleural pressure. Doses
which exert a markedly depressive influence on the respiratory center have, however, the dangers which we have just described. It is of interest in this connection that Prickman has also reported a case of asthma that became moribund after the administration of morphine and that finally recovered with the inhalation of helium and oxygen.

Although we have no clinical or experimental observations on the production of acute pulmonary edema through irritant gases it may be pointed out that the earliest case on record in which positive pressure respiration was used was in a patient who developed edema of the lungs following ingestion and inhalation of carbolic acid. In this remarkable report there was a clearance of edema after an hour’s treatment. This manifestly suggests its use in the treatment of pulmonary edema caused by irritant gases such as chlorine in commercial use and phosgene and other gases employed in war gas poisoning. This type of edema can be ascribed to increased permeability of the capillary wall due to irritation and inflammation.

SUMMARY

Acute pulmonary edema has been studied from an experimental and clinical point of view. Three pathogenetic factors have been discussed:

1. Alterations in the pressure within the lung.
   a. A prolonged pathologically elevated negative chest pressure.
   b. An abrupt termination of backward pressure against the pulmonary capillaries.
2. Left ventricular failure.
3. Increased permeability of the capillary walls.

Following the production of tracheal stenosis it has been shown that edema of the lungs takes place associated with a marked elevation in intrapleural negative pressure. The pathological physiology thus produced exerts a two-fold influence:

   a. A direct suction action on the pulmonary capillaries increasing the tendency to ooze serum through their walls.

   b. A promotion of the inlet of blood into the right heart and a retardation of the flow of blood from the chest into the extrathoracic aorta, factors which increase pulmonary congestion. These physiological events are comparable to what takes place clinically in asthma and dyspnea due to obstructive lesions in the respiratory tubal passages.

As a result of large doses of morphine respiratory effort may be abruptly diminished. Although this makes for a reduction of the intrapleural negative pressure during inspiration, it also takes away the backward pressure which has been previously exerted against the capillaries lining the alveolar walls, as the patient attempts to deliver air through narrow bronchi and bronchioles. Expiration is proportionately much longer than inspiration and the removal of this accustomed back pressure has been found to result in pulmonary edema. Similarly, the removal of long standing obstruction
of the larynx by tracheotomy has been shown to result in an oozing of sero-mucous fluid. The application of positive pressure restores the accustomed backwardly directed pressure and prevents further oozing of serum from the capillary walls.

The experimental production of pulmonary edema in rabbits after intravenous injection of adrenalin has been shown to be due mainly to a left ventricular failure. Under these circumstances no elevation of the negative pressure within the intrapleural cavity was found. It was shown that the left heart was contracted, that the right heart was dilated; disproportion between the output of the two ventricles was, therefore, assumed. A marked passive congestion takes place in these animals followed first by passage of red corpuscles and later serum into the alveolar cells. An increased hydrostatic pressure in the pulmonary capillaries may be assumed under these circumstances to be the main factor, contributory factors being increased capillary permeability due to anoxemia and distention of the capillary walls. This type of experimental pulmonary edema appears to be comparable to that which follows left ventricular failure in clinical disease.

Concerning the third factor, there is evidence that anoxemia, inflammation, and distention of the walls of the capillaries increase capillary permeability. In cases exposed to irritant gases it may be assumed that increase in capillary permeability due to irritation and inflammation is of predominant importance.

Physiological observations were made on the effect of positive pressure respiration on normal subjects, on patients with congestive heart failure and a miscellaneous group. It was shown that when respiration is conducted under a positive pressure of 6 cm. of water normal individuals show a slight elevation in venous pressure, approximately 20 mm. of water and a prolongation of the circulation time of approximately 3½ seconds. In patients with congestive heart failure the venous pressure is increased, in some instances as much as 60 mm. of water and the circulation time may be prolonged 10 to 15 seconds. The heart under these circumstances deals with a smaller volume of blood, due to the fact that the positive pressure within the chest prevents the customary entrance of blood into the right auricle. Explanation of the difference between the behavior of normal subjects and persons with congestive heart failure was listed as follows:

1. The diminished elasticity of the congested lung prevents a compensating rise in negative pressure within the chest which is theoretically possible for the normal individual.

2. The positive pressure within the chest creates a greater interference with diastolic filling of the diseased heart, as compared to the normal.

The marked prolongation of circulation time found in some cardiac patients is not necessarily looked upon as a harmful influence since the decreased volume of blood with which the heart works may be helpful in restoring its function, despite the fact that greater back pressure is present in the systemic veins. Tourniquets applied to the extremities similarly
reduce the amount of blood entering the heart, a procedure which has been found of special value in treating edema of the lungs and "cardiac asthma."

The use of positive pressure respiration in 8 clinical cases of edema of the lungs is described. The effect of the procedure was in most instances a swift clearance of edema and a betterment of the state of circulation. The function of positive pressure in these cases, as in the experimental production of pulmonary edema, was to exert a direct opposing physical force on the external capillary wall tending to counteract the tendency to ooze serum and to decrease the inlet of blood into the right heart, in that way diminishing pulmonary congestion and permitting the heart to work on a smaller volume of blood. An attempt was made to discuss the importance of the factors which have been outlined in each individual case.

CONCLUSION

Acute pulmonary edema has been studied from an experimental and clinical point of view. In cases of respiratory obstruction the pathologically elevated negative pressure within the chest exerts a suction action on the pulmonary capillaries resulting in a tendency to ooze serum through their walls. Expiration against a constricted bronchial passageway maintains a backward pressure against the pulmonary capillary wall, inhibiting the leakage of edema fluid. A sudden termination of obstructive dyspnea, through excessive doses of morphine or as a consequence of tracheotomy, may be followed by edema fluid in the tracheo-bronchial tree. Positive pressure respiration has been found clinically helpful in the treatment of pulmonary edema associated with respiratory obstruction.

The pathogenesis of acute pulmonary edema arising as a complication of heart failure seems best explained by the original hypothesis of Welch: "A disproportion between the working power of the left ventricle and of the right ventricle of such character that the resistance being the same the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." Positive pressure decreases the amount of blood entering the right heart and in that way diminishes pulmonary congestion and facilitates the clearing of pulmonary edema. When the lungs are distended from without by positive pressure there are the additional effects (a) a lowering of the negative pressure within the chest during inspiration and (b) a direct opposing physical pressure on the pulmonary capillaries, especially during expiration.

When pulmonary edema is due to irritation and inflammation, resulting in an increased permeability of the pulmonary capillary walls, positive pressure respiration is at times less effective in clearing the signs of edema.

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