Hyperbaric Oxygenation (OHP) in Massive Pulmonary Embolism*

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Despite the recent advances in cardiovascular surgery, pulmonary embolism remains one of the most serious postoperative complications. All efforts should be directed at eliminating the factors that contribute to its incidence. Recently, there has been a revival of interest in its treatment after Cooley and Beall1 reported the first successful pulmonary embolectomy using cardiopulmonary bypass in 1961. Around the same time hyperbaric oxygenation (OHP) was found beneficial in anoxic states, such as carbon monoxide poisoning, peripheral vascular insufficiency and vascular collapse. Since arterial desaturation and tissue anoxia constitute the main sequelae of massive pulmonary embolism, an experimental model was designed to simulate the clinical picture and study the effects of OHP on the biochemical, electrocardiographic changes, and survival rate of such a model. In addition, embolectomy using cardiopulmonary bypass was evaluated as a definitive therapeutic measure for pulmonary embolism.

**Material and Methods**

Various substances and methods have been used to reproduce pulmonary embolism experimentally. In most instances, foreign material has been used: Barium sulfate, lead phosphate agar, methyl methacrylate (Lucite) spheres, Penrose drains, glass beads, starch granules, amniotic fluid, filter paper, cotton fibers, lycopodium spores, seeds, wax, autogenous fibrin, etc. Besides, general anesthesia utilizing pentobarbital was used uniformly. We believe these two factors modify the experimental model to such a degree that it no longer represents the clinical picture as it occurs spontaneously. Nash and associates2 demonstrated a significant fall in cardiac outputs amounting to 44 per cent of control values, in dogs subjected to the usual anesthetic dose of 30 mg./kg. of sodium pentobarbital. In addition, the depressant effect of barbiturates on respiration is well known to warrant further discussion. Therefore, we decided to use fresh blood clots and local anesthesia. Thirty-two mongrel dogs with an average weight of 11 kg. were mildly sedated with morphine sulfate, 1.5 mg./kg. body weight, given two hours prior to the injection of the clot. Aseptic technique was observed throughout the procedure. Under local 1 per cent procaine anesthesia, the right carotid artery and external jugular veins were cannulated for monitoring arterial pressure, central venous, or pulmonary artery pressures, and injection of the clot into the right side of the heart. The clot was made by aspirating blood 2.3 ml./kg. body weight and allowing it to stand for one hour in a polyethylene tubing one-half inch wide. The latter was then connected snugly to a Bardic catheter (No. 16-18) already inserted in the external jugular vein, and the clot injected manually using a 50 ml. syringe filled with saline. The electrocardiogram was also monitored during the procedure. Arterial and mixed venous blood samples were drawn before injection of the clot, immediately after injection, and at intervals thereafter depending on the fate of the animal. The samples were examined for pH, CO₂ content, hematocrit, lactic acid, pyruvate, and oxygen saturation. The pCO₂ and plasma bicarbonate were calcu-

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lated from the Singer and Hastings nomogram.

**The Oxygen Chamber**

The animals treated with OHP were cannulated as in the control group, fastened to a wooden board and introduced into the pressure chamber. After injection of the clot, the chamber was pressurized with oxygen to three atmospheres absolute within five minutes; they were maintained under pressure for about 15 minutes after which they were decompressed gradually. The total time of exposure to OHP was 30 minutes or shorter, depending on the outcome of therapy.

The pressure chamber used in these experiments consisted of a converted autoclave, already described in detail in a previous publication.*

**Results**

The control group as well as the high pressure oxygen group consisted of 16 dogs each.

A. **Hemodynamic changes** (Fig. 1)

According to the changes in the mean systemic arterial pressure, four patterns were discernible:

Pattern I. A moderate to marked rise which occurred within 15 seconds of clot injection, remained sustained for a few minutes, and then returned to precLOT levels within five minutes.

Pattern II. A moderate drop down to 40-60 mm.Hg within seconds of clot injection, which was not sustained, but returned to baseline levels within two minutes.

Pattern III. An instantaneous drop to zero levels which never recovered.

Pattern IV. A gradual drop to nonrecordable pressures which remained sustained for about two to three minutes followed by a marked rise to hypertensive levels which gradually returned to pre-clot levels.

It was possible to measure the central venous (CVP) or pulmonary pressures (PAP) in the control group, whereas in the OHP group measurements of the CVP or PAP were not possible while the animals were in the chamber. An immediate and marked rise was observed in the CVP, right ventricular pressure and pulmonary artery pressure upon injection of the clot simultaneously with a marked drop in the carotid arterial pressure as illustrated in Fig. 2. In the animals that survived, the pressures were reversed toward their normal values within two minutes. In the animals that died, the CVP and PAP rose immediately above 75 mm.Hg while the

![Graph representing patterns of hemodynamic changes following impact of pulmonary embolus. C=Control, OHP=High Pressure Oxygen](image_url)

**Figure 1:** Graph representing patterns of hemodynamic changes following impact of pulmonary embolus.
Tracings of E.K.G. (Lead II), carotid artery pressure (CAP) and central venous pressure (CVP) before, during and after embolus. Control survival.

Figure 2: Graphs representing changes in the electrocardiogram, carotid artery, right ventricular, and central venous pressures before, during and after embolus, in two control animals.

Figure 3: Tracings illustrating the effect of OHP on the electrocardiogram (Lead II) of an embolized dog.
carotid artery pressure dropped significantly. This trend continued for three to four minutes, after which both pressures dropped to zero levels.

B. Electrocardiographic changes

Most of the animals exhibited sinus bradycardia and arrhythmia prior to clot injection which was attributed to morphine. Upon injection of the clot, sinus tachycardia appeared with frequent premature ventricular systoles. Marked ST depression appeared with inversion of the T wave. Atrial fibrillation was occasionally seen. Terminally, nodal or idioventricular rhythms appeared which ended in ventricular fibrillation or cardiac arrest.

In the control animals that survived, the same electrocardiographic changes appeared after injection of the clot; these persisted for about three to four minutes, then returned gradually to the pre-clot pattern.

In the OHP group, sinus tachycardia, ST depression, varying degrees of AV block with peaked T wave appeared within seconds after clot injection. However, in two to four minutes as the pressure was built up to three atmospheres, bradycardia appeared, the ST depression returned to isoelectric levels and the ECG returned to normal patterns in the surviving animals. In one interesting experiment illustrated in Fig. 3, ST segment became depressed 20 seconds after the impact of the embolus, and idioventricular rhythm appeared one minute later. OHP was started two minutes after injection of the embolus. A notched P wave appeared with marked depression of the ST segment. In four minutes, a normal electrocardiographic pattern reappeared. The tank ran out of oxygen, however, and the pressure within the tank could not be maintained because of leaks. Within six minutes, the T wave became flattened, and in eight minutes the ST segment became elevated. The dog developed complete atrioventricular block with idioventricular rhythm in ten minutes.

C. Biochemical changes

Significant reduction in arterial and mixed venous oxygen saturation associated with a decrease in pH, elevation in lactic acid and a decrease in pCO2, (though it became elevated terminally) were noted in the control group that did not survive (Fig. 4). Similar but less striking changes were

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![Graphs showing changes in pH, pCO2, plasma bicarbonate, oxygen saturation, lactic acid and pyruvate following pulmonary embolus. Group III.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21410/)
observed in the control group that survived. A tendency towards normal values was observed in the recovery period (Fig. 5).

The biochemical changes observed in the OHP group were remarkable in the absence of arterial and mixed venous oxygen desaturation. The mixed venous blood was bright red and oxygen bubbles developed as soon as the samples were exposed to atmospheric air. The changes in pH, pCO₂, and lactic acid as illustrated in Fig. 6 reflected adequate oxygenation of the tissues, in contrast to the anoxic and acidotic changes seen in the control group.

D. Survival rate

Of the 16 animals comprising the control group, eight survived giving a rate of 50 per cent. Among the 16 animals treated with OHP, there were five fatalities with 11 survivors, giving a rate of 69 per cent. Although the series is too small to make the difference in survival rate statistically significant, further analysis of the data sheds more light on the value of OHP. From a hemodynamic point of view, animals exhibiting patterns I and II would have survived without any therapy. There were seven controls and two OHP in those groups, all of which survived. Those animals which exhibited marked systemic hypotension rarely recovered. In this study (patterns III and IV), nine control and 14 OHP dogs followed that pattern. There were nine survivals in the OHP group and three in the control group, giving a survival rate of 64 per cent in the OHP group compared to 33 per cent in the control group.

DISCUSSION

Despite a large amount of experimentation, much controversy still exists regarding the mechanisms operating after a massive pulmonary embolus. Niden and Aviado, using glass beads to produce pulmonary embolism, concluded that at least three components were responsible for the hemodynamic changes: (1) primary mechanical obstruction of the vessels which produces the immediate rise in pulmonary artery pressure, (2) secondary local vasoconstric-
tion, and (3) vasoconstriction extending to the other lobes. Williams,\textsuperscript{4} utilizing the same technique of glass spheres and isolated perfusion of the left lower lobe, concluded that the hemodynamic effects were due to mechanical obstruction to the flow of blood through the lungs and were eventually followed by right heart failure. Nelson and Smith\textsuperscript{7} found insufficient evidence that neurogenic reflexes play any role in massive embolism. Serotonin\textsuperscript{8} (5-hydroxy-tryptamine) has also been implicated in the production of pulmonary hypertension and systemic hypotension, since it produces these same hemodynamic changes when injected intravenously and is present in the blood clot and possibly in the lungs. Parmley, North and Ott\textsuperscript{9} stated that the cause of severe but potentially reversible systemic hypotension appeared to be due to a combination of factors including a decrease in cardiac output and reflex changes that influence the systemic arteriolar resistance.

Despite this controversy regarding the pathophysiologic mechanisms of massive pulmonary embolism, there is unanimous agreement about the resulting peripheral arterial desaturation, anoxemia, and the beneficial effects of oxygen. In 1936, Gibbon and Churchill\textsuperscript{10} found that when 86 per cent of the pulmonary vascular bed was occluded, there was a fall in systemic blood pressure and a profound decrease in the oxygen saturation of the arterial blood resulting in death. Inhalation of oxygen increased the oxygen saturation of the blood and maintained life of the animals. According to Binger and co-workers\textsuperscript{11} this arterial desaturation was brought about by the congestion of the pulmonary vessels and the rapid flow of blood resulting in impaired diffusion of oxygen into the blood. In 1939, De Takats and associates\textsuperscript{12} produced fatal pulmonary emboli by the injection of 2 ml. of an emulsion of potato starch into the central vein of the ear of the rabbit. When oxygen was administered through a tracheal tube, it reduced the dyspnea and protected the whole series from death.

Niden and Aviado\textsuperscript{13} considered the anoxemia a potential cause of death and a reasonable direction for therapeutic intervention. The average fall in arterial oxygen content after embolization in 12 dogs amounted to three volumes per cent. The fall was often maximal within five minutes after embolization, and was considered too soon to be produced by a change in the permeability of the alveolar membrane.

Figure 6: Graphs showing changes in pH, pCO\textsubscript{2}, oxygen saturation, lactic acid, and pyruvate following pulmonary embolus and OHP.
Forced ventilation with air did not appreciably alleviate the anoxemia, but administration of 100 per cent oxygen led to prompt and complete removal of the anoxemia. This relief, however, could not be maintained for more than about 30 minutes after which anoxemia reappeared and the animals died despite continuous oxygen administration. From their perfusion experiment they concluded that pulmonary arteriovenous communications existed and were at least 420 micron in size. Ventilation of the lungs with 100 per cent oxygen decreased the number of these communications, while 10 per cent oxygen increased it. Williams' noted a 35 per cent fall in oxygen saturation in 31 experiments on dogs breathing room air under constant positive respiration. However, repeated observations of the oxygen saturation on 23 dogs breathing oxygen revealed no significant fall. He did not believe that the unsaturation seen after embolism was due to a form of venous admixture to arterialized blood since a shunt of 50 per cent or greater would have been necessary to cause such a degree of unsaturation. The most likely explanation was the reduction in diffusion capacity of the lung, which improved as new capillaries opened and the area available for gas exchange increased.

Our data corroborate the above conclusions. The hyperbaric oxygen prevents the arterial desaturation and anoxemia of the tissues, not only by increasing the amount of dissolved oxygen in the plasma, but also by facilitating oxygen diffusion. This supports the function of the cardiopulmonary system during the sudden hemodynamic changes that follow the impact of the embolus, until compensatory mechanisms are activated. The quick reversal of the hemodynamic, biochemical and electrocardiographic changes following OHP administration, as well as the gross and microscopic pathology findings confirm this assumption. It was noted that when the right ventricle and the main pulmonary artery with its two major branches were occluded with clots, the chances of survival were very poor in both the control and OHP groups. The pathologic findings of these animals were correlated with the hemodynamic and ECG findings and it became apparent that the instantaneous cardiovascular collapse following injection of the embolus did not afford the animal an opportunity to compensate and survive. However, in the OHP treated group, the heart maintained its function and was able to displace the clots peripherally into the pulmonary circuit where the capillary surface area is much larger than that of the pulmonary artery.

Although hyperbaric oxygenation can be complicated by oxygen toxicity, the short period of treatment, as well as the moderate pressure used avoided such complications. The surviving animals treated with OHP did not exhibit any neurologic sequelae, although two dogs became acutely agitated and aggressive immediately following decompression. The development of congestion and atelectasis of the lungs as seen in the histologic sections was attributed to the massive embolus and not to oxygen toxicity since it occurred to the same extent in both groups.

Despite significant improvement obtained experimentally with oxygen therapy of pulmonary embolism, we do not advocate it as the treatment of choice. Prevention of pulmonary embolism by adequate anticoagulation and vena cava ligation remains the ideal method. However, when it does occur, embolectomy using the pump oxygenator is the definitive treatment. We evaluated this approach in eight animals and were able to recover most of the emboli. Hyperbaric oxygenation, however, should be considered a supportive therapy in all cases of massive pulmonary embolism. Further experimentation is in progress to evaluate the feasibility of embolectomy following irreversible pulmonary embolization treated with hyperbaric oxygenation.

**Summary**

Massive pulmonary embolism was produced in 16 dogs using autologous blood
clots. Survival rate in this group was 50 per cent. Sixteen dogs were embolized in a similar fashion and were treated with oxygen under three atmospheres absolute. The survival rate was increased to 69 per cent. The improvement in survival rate was correlated with improvement in the hemodynamic, biochemical and electrocardiographic changes.

ACKNOWLEDGMENT: We gratefully acknowledge the technical assistance of George Henning, and the help of Doctor Yu Chen Lee in the interpretation of the electrocardiograms.

RESUMEN
Se produjo embolia pulmonar masiva en 16 perros usando coágulos de su propia sangre. La sobrevida fue de 50 por ciento. Se produjeron embolias de manera similar en 16 perros y fueron tratados con oxígeno bajo tres atmósferas. La sobrevida ascendió a 69 por ciento. La mejoría de la sobrevida estuvo en relación con cambios hemodinámicos, bioquímicos y electrocardiográficos.

RESUMÉ
Une embolie pulmonaire massive fut provoquée chez 16 chiens, en utilisant des caillots de sang. Le taux de survie dans ce groupe fut de 50%. 16 chiens furent soumis à l’embolie de la même façon et furent traités par l’oxygène sous pression de trois atmosphères. Le taux de survie est en corrélation avec l’amélioration des modifications hémodynamiques, biochimiques et électrocardiographiques.

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REFERENCES

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BIFID STERNUM

A case of a rare congenital defect, bifid sternum, in a woman aged 30 is reported. An acrylic plaque was used to close the defect, since the patient's skeletal development did not permit approximation of the sternal halves, and in view of her refusal to accept any plastic repair that required osseous or cartilaginous grafting. The phylogenetic, embryologic and roentgenologic diagnosis and the treatment of congenital sternal defects are discussed. A new technique for repair of bifid sternum is described.