# INFLUENCE OF CARBON DIOXIDE ON THE INCIDENCE OF VENTRICULAR FIBRILLATION IN HYPOTHERMIA

By

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In 1950, McQuiston[11] reported the clinical use of hypothermia to reduce body oxygen demands in 128 patients undergoing cardiac surgery. In the same year Bigelow et al.[4] published his experimental work on hypothermic dogs and suggested the future clinical use of hypothermia for more complex heart surgery. In 1953 Lewis and Taufic[10], followed shortly by Cookson, Neptune, and Bailey[8], first performed successfully open intracardiac surgery under hypothermia. Previous to this time generalized hypothermia was confined to abortive experimental efforts to control malignancies[19].

Since 1950, following the experimental work on hypothermic dogs by Bigelow's group[3], an association between hypothermia and ventricular fibrillation has been recognized. The possibility of this arrhythmia has impeded the clinical application of hypothermia. In 1947, Beck et al.[1] performed the first clinically successful defibrillation. Since that time defibrillation has been accomplished quite frequently; however, the onset of ventricular fibrillation still signifies considerable danger to the patient because the interruption of this arrhythmia is not invariably successful and it may recur. In spite of this danger hypothermia has attained widespread use in the repair of certain congenital heart defects and vascular surgery.

The successful clinical application of the pump oxygenator has superceded to a certain extent the urgent need for hypothermia. However hypothermia possesses certain advantages. Relatively fewer doctors, nurses, and technicians, less complex and expensive equipment, and a markedly decreased amount of fresh whole blood represent advantageous aspects of hypothermia. The refinement of hypothermia may possibly provide smaller medical centers with the means to safely perform some cardio-vascular surgery.

Much effort has been expended attempting to elucidate the mechanism, therapy, and prophylaxis of ventricular fibrillation. Extensive studies have been conducted related to the effects of local anesthetic agents, procaine amide, quinidine, autonomic drugs, and electrolytes on the incidence of ventricular fibrillation.[6,12] Covino et al.[9], Bigelow et al.[4], and Riley et al.[15] have investigated various anesthetic agents and their relationship to the incidence of ventricular fibrillation in hypothermia. Ventilation and the concentration of oxygen and carbon dioxide in the administered gas have aroused some controversy.

Lewis and Niazi[13] noted that heart block in hypothermic rats and dogs and ventricular fibrillation in hypothermic dogs could be prevented or significantly reduced by adding carbon dioxide to the inspired gas

mixture. The same author[14] and Bigelow et al.[3] suggested that respiratory alkalosis, produced by ventilation with 100% oxygen during hypothermia, causes a decreased tissue oxygen tension due to the shift to the left of the oxy-hemoglobin dissociation curve. Lewis and Niazi further reported that the maintenance of a constant pH, at a level slightly below normal by administering carbon dioxide with an artificial respirator, reduces the incidence of arrhythmias in hypothermia. Evidence that a rapid drop in alveolar carbon dioxide may cause ventricular fibrillation in the normothermic dog has been presented by Brown and Miller[5].

On the other hand Beecher[2] has suggested that high carbon dioxide levels in the face of adequate oxygen levels may produce deleterious reflex vagal activity. Hypoxia and hypercapnia produced a higher incidence of cardiac arrest on vagal stimulation than did hypoxia alone according to Sloan.[16] Young et al.[20] observed that hypercapnia enhances and hypoxia diminishes the effect of vagal stimulation on the heart. It has been found by Stewart, Virtue, and Swan[17] that cardiac arrest by vagal stimulation was enhanced by hypercapnia in the normal animal. They further find that hypercapnia slows the heart beat. In chronic hypoxia, hypercapnia does not enhance vagal arrest. Chronic hypoxia predisposes to ventricular fibrillation on vagal stimulation. In other

studies Swan et al.[18] presented experimental evidence that hyperventilation with 100% oxygen reduces the incidence of ventricular fibrillation in hypothermia.

This investigation is concerned with the physiological factors influencing ventricular fibrillation. Special attention was paid to the role of carbon dioxide in view of the divergence of opinion of Swan's group and Lewis's group.

## Procedure

Dogs of varying ages weighing between five and twenty kilograms were anesthetized with different anesthetic agents (sodium pentobarbital, 25-30 mgm/kgm, and a combination of lidocaine, 15 mgm/kgm, and sodium thiopental, 15 mgm/kgm). Continuous and simultaneous blood pressure and electrocardiographic recordings were obtained by the use of a strain gauge and a twin channel electrocardiograph. Tracheal intubation was accomplished and artificial respiration instituted by means of a pneumatic balance resuscitator. After partial removal of the animals' hair they were placed in a tub of ice water. Temperatures were observed by means of a Yellow Springs Tele-Thermometer, with the thermocouple inserted well into the rectum. Succinylcholine, 2-10 mgm, was administered intravenously to prevent shivering. Gas mixtures were administered with an anesthesia machine.

Under close observation the animals remained in the ice bath until a temperature two degrees above the desired hypothermic level was attained. The temperature usually continued downward one or two degrees after removal from the ice water. Blood specimens were withdrawn from the femoral artery at the desired level of hypothermia or at the onset of ventricular fibrillation.

If at any point ventricular fibrillation

occurred an immediate thoracotomy was performed through the fourth left intercostal space. In the absence of spontaneous fibrillation an elective thoracotomy was accomplished after the desired hypothermic level was reached. With the heart exposed a standard routine of cardiac stimulation was employed: 1) the epicardium was stroked ten times with the blunt handle of a scalpel, 2) the heart was manually massaged for thirty seconds, 3) after a one minute interval the massage was repeated. In the absence of ventricular fibrillation the animal was warmed in a water bath at 45 degrees C. and the thoracotomy was closed.

If ventricular fibrillation occurred at any point lidocaine was employed, as described by Carden and Steinhaus[7], in an attempt to interrupt the fibrillation. Sustained interruption of fibrillation with adequate cardiovascular function as judged by electrocardiogram and blood pressure was designated as resuscitation. Survival for twenty four hours constituted recovery.

One hundred and twelve animals were employed in eleven different series. Preliminary work consisted of two series in which an elective thoracotomy was not performed. In the remaining series various gas mixtures (100% oxygen, 5% carbogen, and 10% carbogen), different anesthetic agents, and two levels of hypothermia (20° C. and 27° C.) were compared. In one series 0.4 cc of a

1:4000 solution of prostigmine was administered intravenously at 25° C. and 0.2 cc of the same solution was injected into the left ventricle with the aorta occluded at 20° C.

## Results

Table I discloses the results of preliminary studies in which animals were cooled to 20° C. under pentobarbital anesthesia. In both the series using 100% oxygen and the series using 10% carbon dioxide 3 of 10 of the animals developed ventricular fibrillation. Of the 3 fibrillations in the first group, one animal developed asystole which eventuated in fibrillation with resuscitative measures. Two of the three fibrillations in the second group followed resuscitation of asystole. In the first series the average carbon dioxide content of the arterial blood was 27.2 volumes percent and the oxygen was 24.3 volumes percent. In contrast the animal receiving 10% carbon dioxide had an average blood level of carbon dioxide of 60.8 volumes percent and an oxygen level of 21.7 volumes percent.

Table II demonstrates the results of studies on mechanical stimulation of the hypothermic heart under pentobarbital anesthesia. Eight of ten animals receiving 100% oxygen developed ventricular fibrillation--three following resuscitation of asystole. Of the ten animals receiving 10% carbon dioxide, nine developed ventricular fibrillation with one of the nine fibrillating after asystole. In the series employing 5% carbon dioxide nine of 10 animals fibrillated while no animals developed asystole. The animals receiving 100% oxygen

had an average arterial carbon dioxide level of 30.4 volumes percent and an oxygen level of 19.8 volumes percent. The series receiving 10% carbon dioxide showed average blood levels of carbon dioxide of 62.5 volumes percent and oxygen levels of 19.1 volumes percent. The series of animals in which 5% carbon dioxide was administered showed respective carbon dioxide and oxygen blood levels of 58.1 and 18.6 volumes percent.

Table III lists the results of mechanical stimulation of hypothermic hearts under lidocaine-thiopental anesthesia. Four of 12 dogs receiving 100% oxygen fibrillated--one following resuscitation of asystole. In the series employing 5% carbon dioxide 4 of 10 also exhibited ventricular fibrillation; however none of these fibrillations were preceded by asystole.

In the first series the average carbon dioxide content of the blood was 27.1 volumes percent and the oxygen was 22.7 volumes percent. Average carbon dioxide and oxygen levels for the second series proved to be 58.2 volumes percent and 22.7 volumes percent.

Table IV tabulates the results of mechanical stimulation of the heart at 27° C. under lidocaine-thiopental anesthesia. One of 10 animals fibrillated while receiving 100% oxygen and 2 of 10 fibrillated while receiving 5% carbon dioxide. No asystole was observed. In the first series the average blood carbon dioxide

was 36.0 volumes percent and the average blood oxygen was 21.3 volumes percent. In contrast the second series showed respective carbon dioxide and oxygen levels of 55.0 and 22.2 volumes percent.

Of 10 animals receiving prostigmine 7 fibrillated. The average blood carbon dioxide and oxygen levels were 31.0 and 20.0 volumes percent respectively.

TABLE I

HYPOTHERMIA TWENTY DEGREES CENTIGRADE

Pentobarbital Anesthesia

| Gas Mixture | Number of Dogs | Average Arterial $CO_2$ | Average Arterial $O_2$ | Asystole | Ventricular Fibrillation After Asystole | Ventricular Fibrillation Directly | Ventricular Fibrillation Total |
|---|---|---|---|---|---|---|---|
| 100% $O_2$ | 10 | 27.2 vol % | 24.3 vol % | 1 | 1 | 2 | 3 |
| 10% $CO_2$ | 10 | 60.8 vol % | 21.7 vol % | 2 | 2 | 1 | 3 |

TABLE II

MECHANICAL STIMULATION OF THE HEART

HYPOTHERMIA TWENTY DEGREES CENTIGRADE

Pentobarbital Anesthesia

| Gas Mixture | Number of Dogs | Average Arterial $CO_2$ | Average Arterial $O_2$ | Asystole | Ventricular Fibrillation After Asystole | Ventricular Fibrillation Directly | Ventricular Fibrillation Total |
|---|---|---|---|---|---|---|---|
| 100% $O_2$ | 10 | 30.4 vol % | 19.8 vol % | 4 | 3 | 5 | 8 |
| 10% $CO_2$ | 10 | 62.5 vol % | 19.1 vol % | 1 | 1 | 8 | 9 |
| 5% $CO_2$ | 10 | 58.1 vol % | 18.6 vol % | 0 | 0 | 9 | 9 |

TABLE III

MECHANICAL STIMULATION OF THE HEART

HYPOTHERMIA TWENTY DEGREES CENTIGRADE

Lidocaine-Thiopental Anesthesia

| Gas Mixture | Number of Dogs | Average Arterial $CO_2$ | Average Arterial $O_2$ | Asystole | Ventricular Fibrillation After Asystole | Ventricular Fibrillation Directly | Ventricular Fibrillation Total |
|---|---|---|---|---|---|---|---|
| 100% $O_2$ | 12 | 27.1 vol % | 22.7 vol % | 3 | 1 | 3 | 4 |
| 5% $CO_2$ | 10 | 58.2 vol % | 22.7 vol % | 1 | 0 | 4 | 4 |

TABLE IV

MECHANICAL STIMULATION OF THE HEART

HYPOTHERMIA TWENTY SEVEN DEGREES CENTIGRADE

Lidocaine-Thiopental Anesthesia

| Gas Mixture | Number of Dogs | Average Arterial $CO_2$ | Average Arterial $O_2$ | Ventricular Fibrillation Total |
|---|---|---|---|---|
| 100% $O_2$ | 10 | 36.0 vol % | 21.3 vol % | 1 |
| 5% $CO_2$ | 10 | 55.0 vol % | 22.2 vol % | 2 |

## Discussion

Similar incidences of ventricular fibrillation were observed with intact dogs which were cooled to 20°C. and administered either 100% oxygen or 10% carbon dioxide. In view of the relatively low rate of ventricular fibrillation, in the intact animal in the preliminary series, mechanical stimulation of the heart was employed in the subsequent series.

Introduction of mechanical stimulation of the heart produced a high incidence of ventricular fibrillation as is shown in Table II. This increase was uniformly noted using 100% oxygen, 10% carbon dioxide, and 5% carbon dioxide. It is interesting to note that similar high rates of ventricular fibrillation were obtained irrespective of the concentration of carbon dioxide administered. It was observed that asystole tended to occur more frequently when 100% oxygen was used, however fibrillation often ensued with attempted resuscitation. Adequate oxygenation was demonstrated in all series. High carbon dioxide levels were demonstrated when both 10% carbon dioxide and 5% carbon dioxide were used.

The use of lidocaine-thiopental anesthesia with cardiac stimulation resulted in a lower proportion of ventricular fibrillation as summarized in Table III. The incidences were similar for both 100% oxygen and 5% carbon dioxide. Again a greater number of animals receiving

100% oxygen developed asystole.

At hypothermic levels of 27°C. the incidence of ventricular fibrillation was markedly lower than at 20°C. It is interesting to note that the range of hypothermia used clinically is 27° to 30°C. No great difference was observed when carbon dioxide and oxygen were compared. There is general agreement that lower temperatures are associated with a greater incidence of cardiac asystole and ventricular fibrillation. Other complications that occur are auricular fibrillation, varying degrees of heart block due to increased conduction time, and hemostatic problems due to increased bleeding and coagulation times.

The results of Tables I, II, and III do not support the views of either Swan or Lewis. Proponents of carbon dioxide advocate a stable, low normal pH of the blood. They suggest that the tissues are bathed in a higher oxygen tension, by virtue of the favorable effects on the oxyhemoglobin dissociation curve, by a medium of low pH. Hyperventilation with 100% oxygen has less undesirable reflex vagal activity according to Swan's group.

The question of whether to use 100% oxygen or a carbon dioxide and oxygen mixture during hypothermia is not answered by the conflicting reports in the literature. The results of this study do not delineate the effects of carbon dioxide into beneficial or detrimental

catagories. Absence of fibrillation was noted in individual dogs with carbon dioxide levels as high as 62.6 vol. % and as low as 25.6 vol. %. In view of the clinical and experimental successes with either method it is evident that carbon dioxide may not be the deciding factor in the production of arrhythmias during hypothermia. Other factors, associated with the incidence of ventricular fibrillation, are concerned with the vigorousness of manipulation of tissue, electrolyte imbalance, surgical experience, anesthetic agents, and biological difference in response to stimulation.

## Conclusions

Mechanical stimulation of the hypothermic dog's heart increased the incidence of ventricular fibrillation. The question of whether to use 100% oxygen or a mixture of carbon dioxide and oxygen, during hypothermia, cannot be resolved on the basis of this study of 112 dogs. It is suggested that carbon dioxide blood levels are not as important a factor in ventricular fibrillation as was previously indicated.

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