Cardiac Metabolism in Experimental Ventricular Fibrillation


The cardiac metabolism of the fibrillating left ventricle of the dog heart with and without maintenance of left coronary artery inflow was investigated. During ventricular fibrillation without maintenance of coronary flow, myocardial adenosine triphosphate and glycogen fell progressively, and in vitro oxygen consumption of biopsied tissue initially increased, but with adequate coronary perfusion these elements were maintained. With reinstigation of coronary flow after 30 to 40 minutes of fibrillation without flow, resynthesis of high energy phosphate occurred. The coronary artery-coronary sinus oxygen difference and left ventricular oxygen usage both decreased in the perfused fibrillating heart as compared with the values in the beating heart.

The frequent experimental and clinical occurrence of ventricular fibrillation has stimulated much effort in resuscitation methodology and many investigations of the mechanism of fibrillation. More recently, ventricular fibrillation has been induced purposely to facilitate animal intracardiac surgery. Few experimental studies, however, have been concerned with the metabolic changes associated with this state. In 1933, Hooker and Kehar concluded from measurements of dextrose consumption and carbon dioxide output that the carbohydrate metabolism of the dog heart in ventricular fibrillation is increased. Senning, however, recently reported that the cardiac oxygen consumption is the same during ventricular fibrillation and regular sinus rhythm when the coronary and systemic circulations are maintained by an extra-corporeal pump. Wesolowski and colleagues present data which suggest that the level of high energy phosphates in the atrial and right ventricular myocardium is maintained during a prolonged period of ventricular fibrillation with complete myocardial ischemia.

In an effort to establish further the metabolic status of both perfused and nonperfused fibrillating ventricular tissue, several biochemical parameters associated with gross myocardial activity have been studied. These measurements were made before and after the electrical induction of ventricular fibrillation and include coronary artery blood inflow, coronary artery-coronary sinus oxygen difference, cardiac tissue adenosine triphosphate (ATP), glycogen and in vitro oxygen consumption.

EXPERIMENTAL PROCEDURE

Male and female mongrel dogs (9 to 15 Kg.) were anesthetized with intravenous sodium pentobarbital (30 mg. per kilogram of body weight). The chest was opened by removal of portions of the third, fourth, and fifth left ribs, and respiration was maintained through an endotracheal catheter with a compressed air respirator or an oxygen demand type valve apparatus (Pneophore).

The experimental preparation is schematically shown in figure 1. After the pericardium was incised, the left coronary artery was isolated at its aortic origin and a suture passed around it in preparation for cannulation. Blood was led from a trocar in the left carotid artery through a recording rotameter and then into the left coronary artery via a brass cannula. The latter cannula was introduced into the origin of the left coronary artery via the brachiocephalic artery and aorta, and tied in place. Coagulation was prevented by the intravenous administration of heparin, 10 mg./Kg. initially and 5 mg./Kg. every 30 minutes thereafter. By a stopcock arrangement, the coronary artery could also be perfused by a gravity perfusion system with freshly drawn, heparinized, cross-matched, donor dog blood warmed to 37 to 38 C.

Blood samples from the coronary sinus were obtained from a number 7F intravenous catheter inserted 3 to 4 cm. into the coronary sinus via the left external jugular vein. A plastic catheter inserted to the level of the right atrium via the left femoral vein and the inferior vena cava was utilized to bleed...
the animal to maintain approximate blood volume balance whenever donor blood was being introduced through the coronary perfusion system.

Fibrillation was induced by the application of electrical stimuli (20 v., 50 cycles per second) to the myocardium. Defibrillation was effected by single or multiple shocks (110 v., 60 cycles per second, approximately 0.1 second) applied to the heart with large gauze-padded electrodes. Fibrillation was followed visually and electrocardiographically.

Cardiac tissue (200 to 300 mg.) was excised for immediate chemical analysis from a site of the left ventricle whose blood supply had not been previously compromised by a knife incision, and generally the biopsy area was sutured during the interval between tissue sampling.

**CHEMICAL METHODS**

**Adenosine Triphosphate (ATP).** Approximately 30 to 40 mg. of biopsy tissue was extracted immediately after excision with 5 per cent trichloroacetic acid at 0 C. and the adenosine triphosphate was estimated as acid labile phosphate. Values obtained by this method for the dog heart are in close agreement with the adenosine triphosphate content as determined by the more specific spectrophotometric-enzymatic methods.7

**Glycogen.** Glycogen was determined by the method of Good, Kramer, and Somogyi8 as modified by Stadie, Hauggard, and Marsh9 using the Nelson technic for glucose analysis.

**In Vitro Oxygen Consumption.** Approximately 150 mg. of biopsy cardiac tissue slices (0.5 mm. thick) were prepared immediately following excision. Their oxygen consumption was measured in a Warburg manometer apparatus with an oxygen gas phase for approximately 60 minutes at 37 C. The composition of the tissue medium was: NaCl 0.1 M; Na2HPO4, 0.017 M; NaH2PO4, 0.017; pH 6.8.

**Coronary Artery-Coronary Sinus Oxygen Difference.** This difference was calculated from blood saturation determinations made by the spectrophotometric technic of Drabkin and Gordy10 and from blood capacity determinations made by the cyanomethemoglobin technic.11

**RESULTS**

In nine control experiments in which no coronary blood inflow was provided during the period of ventricular fibrillation, biopsies were taken from the left myocardium just before the induction of fibrillation and after 15 minutes and 40 minutes of fibrillation. Vigorous fibrillatory movements were visible immediately following the induction of fibrillation, and the heart maintained moderate tonus for three to five minutes. Then the movements gradually subsided over progressively greater areas, until the time of complete cardiac quiescence (20 to 35 minutes). In these experiments (table 1, Control) in which no coronary blood flow existed during the period of ventricular fibrillation, the levels of cardiac acid labile phosphate (ATP) and cardiac glycogen fell progressively from the control values. The in vitro oxygen consumption of the biopsied myocardial tissue was significantly elevated over the control level after 15 minutes of fibrillation, but after 40 minutes there was no significant difference from the control level.

In nine subsequent experiments (table 1, Perfusion), after inducing ventricular fibrillation, the coronary inflow was immediately re-established by gravity perfusion of the left main coronary artery at approximately the prefibrillatory level of coronary blood inflow. There was no significant decrease in myocardial adenosine triphosphate content, and no significant change in the in vitro oxygen consumption from the control levels even after 40
TABLE 1.—Biochemical Data from Cardiac Biopsy Tissue

<table>
<thead>
<tr>
<th></th>
<th>ATP (acid Labile Phosphate) µM per Gm.</th>
<th>Glycogen µM per Gm. per hr.</th>
<th>O2 Consumption ml/Og/100 Gm. left ventricle/min.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± S.E.M.</td>
<td></td>
<td>Mean ± S.E.M.</td>
</tr>
<tr>
<td>Control (9 dogs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before fibrillation</td>
<td>9.7 ± 0.7</td>
<td>48.6 ± 2.1</td>
<td>44.6 ± 4.4</td>
</tr>
<tr>
<td>After 15 min. fibrillation</td>
<td>6.1 ± 0.6†</td>
<td>33.7 ± 1.4†</td>
<td>60.1 ± 4.9†</td>
</tr>
<tr>
<td>After 40 min. fibrillation</td>
<td>2.6 ± 0.5†</td>
<td>23.2 ± 1.4†</td>
<td>50.8 ± 2.6*</td>
</tr>
<tr>
<td>Perfusion (9 dogs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before fibrillation</td>
<td>9.0 ± 0.7</td>
<td>32.8 ± 6.2</td>
<td>45.2 ± 4.6</td>
</tr>
<tr>
<td>After 15 min. fibrillation</td>
<td>8.1 ± 0.5*</td>
<td>30.9 ± 6.7*</td>
<td>52.7 ± 4.5*</td>
</tr>
<tr>
<td>After 40 min. fibrillation</td>
<td>7.2 ± 0.8*</td>
<td>36.9 ± 3.0*</td>
<td>50.4 ± 3.0*</td>
</tr>
<tr>
<td>Delayed Perfusion (6 dogs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before fibrillation</td>
<td>8.6 ± 0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 30-40 min. fibrillation</td>
<td>3.5 ± 0.6†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 10 min. perfusion</td>
<td>5.3 ± 0.8‡</td>
<td></td>
<td></td>
</tr>
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</table>

* Not significantly different from control value.
† P < 0.01 significantly different from control value (i.e., before fibrillation).
‡ P < 0.05 significantly different from control value (i.e., before fibrillation).

minutes of fibrillation, as long as the left coronary artery blood inflow was maintained. Glycogen levels in the perfused hearts were maintained at the control level for the initial 15 minutes of fibrillation and were not significantly decreased after 40 minutes of fibrillation. In contrast to the nonperfused hearts, vigorous, rapid fibrillatory movements and electrocardiographic fibrillation currents were observed throughout the 40-minute period in the perfused fibrillating hearts.

In a third series of experiments (table 1, Delayed Perfusion) ventricular fibrillation was induced after the control biopsy was obtained from the normally contracting myocardium, and fibrillation was allowed to proceed for approximately 30 minutes with no perfusion of the left coronary artery. A second biopsy was obtained at this time, and then the left coronary blood flow was re-established at approximately the prefibrillatory level via the gravity perfusion system. Almost immediately the quiescent heart resumed vigorous fibrillatory movements. After 10 minutes of perfusion, a third biopsy was secured and defibrillation immediately attempted. In six technically satisfactory experiments, the reinstitution of perfusion resulted in the restoration of vigorous,

TABLE 2.—Oxygen Consumption of Perfused Fibrillating Heart

<table>
<thead>
<tr>
<th></th>
<th>O2 Consumption ml/Og/100 Gm. left ventricle/min.</th>
<th>Coronary A-V O2 Difference ml/Og/100 Gm.</th>
<th>Left Coronary Blood Flow ml/100 Gm. left ventricle/min.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± S.E.M.</td>
<td>Mean ± S.E.M.</td>
<td>Mean ± S.E.M.</td>
</tr>
<tr>
<td>Before fibrillation</td>
<td>11.3 ± 1.1</td>
<td>17.5 ± 0.8</td>
<td>66.3 ± 5.7</td>
</tr>
<tr>
<td>After 15 min. fibrillation</td>
<td>4.8 ± 0.8*</td>
<td>0.9 ± 1.3*</td>
<td>47.9 ± 2.5*</td>
</tr>
<tr>
<td>After 30-40 min. fibrillation</td>
<td>5.6 ± 1.0†</td>
<td>12.4 ± 1.0†</td>
<td>44.3 ± 4.4*</td>
</tr>
</tbody>
</table>

* P < 0.01 significantly different from control value (i.e., before fibrillation).
† P < 0.05 significantly different from control value (i.e., before fibrillation).
rapid fibrillatory movements and a reversal of the downward trend of cardiac acid labile phosphate. In two instances successful countershock restoration of a regular cardiac rhythm was temporarily effected.

The gross oxygen consumption of the left myocardium (left coronary inflow multiplied by coronary artery–coronary sinus oxygen difference) in the beating heart (control) and in the fibrillating heart (after 15 and 40 minutes of fibrillation) was measured in the nine dogs who had left coronary artery inflow maintained by gravity perfusion with donor blood. In eight of the nine experiments (table 2) the coronary artery–coronary sinus oxygen difference was decreased in ventricular fibrillation when left coronary artery perfusion continued for 15 to 40 minutes. In addition the oxygen consumption also decreased, the average reduction being about 50 per cent as compared with the control.

This reduction in left ventricular oxygen consumption and in coronary artery–coronary sinus oxygen difference was also a characteristic early finding after the onset of ventricular fibrillation (fig. 2). In these experiments, left coronary inflow from the gravity bottle was set before fibrillation at approximately the flow rate existing when the left coronary was perfused from the aorta. Measurements of left coronary inflow and coronary artery–coronary sinus oxygen difference were made within three minutes after the induction of ventricular fibrillation, and the computed oxygen consumption fell from the pre-fibrillation control level of 7.5 ml. oxygen per minute per 100 Gm. left ventricle to 4.0 ml. oxygen per minute per 100 Gm. left ventricle, and the coronary artery–coronary sinus oxygen difference dropped from 13.3 to 11.4 ml. oxygen per 100 ml. left coronary blood flow.

**DISCUSSION**

The heart is predominantly an aerobic organ richly supplied with oxygen and substrates and powerfully equipped with respiratory enzymes. It possesses little ability for anaerobic recovery, and in severe myocardial anoxia sudden failure of the heart occurs in association with exhaustion of the reserves of energy-rich phosphates and glycogen.

Our data, in contrast with those of Wesolowski and associates indicate a progressive loss of adenosine triphosphate (acid labile phosphate) in the ischemic fibrillating left ventricle. The glycogen reserves also decrease progressively under these conditions. If, however, an adequate left coronary blood flow is provided during fibrillation by an extracorporeal perfusion system, the myocardial adenosine triphosphate and glycogen content can be maintained during prolonged periods of fibrillation. Furthermore, despite 30 to 40 minutes of ventricular fibrillation with no coronary blood flow and complete myocardial ischemia, the reinstatement of left coronary artery perfusion results in the apparent resynthesis of high energy phosphate and the concomitant restoration of vigorous, rapid fibrillatory movements. At times, successful defibrillation by countershock is possible. Although the anaerobic metabolism of the cardiac glycogen is inadequate to maintain myocardial adenosine triphosphate at normal levels, such anaerobic metabolism may be sufficient to sustain intact, for reasonable periods, the labile enzyme complex responsible for the generation of high energy phosphates.

Much experimental effort has recently been
directed towards the development of techniques for intracardiac surgery. In both the clinical and experimental application of these techniques, ventricular fibrillation has been frequent in occurrence and has been viewed by some as a complication despite the availability of countershock and pharmacologic resuscitation techniques.16 Senning3 and Juvenelle and colleagues,16 however, are of the opinion that prolonged ventricular fibrillation is not dangerous, per se, provided there is adequate myocardial oxygenation. The latter investigators have reported survival of dogs maintained in controlled deep hypothermia with extracorporeal circulatory support after hours of ventricular fibrillation. They point out that defibrillation can always be accomplished if the heart has received adequate oxygenation during the fibrillation period.

We have observed that the perfused fibrillating left heart, even after 40 minutes of fibrillation at body temperature, has a normal adenosine triphosphate content and active, rapid fibrillatory movements in contrast to the ischemic, adenosine triphosphate-depleted, quiescent fibrillating heart. The maintenance of an adequate myocardial level of adenosine triphosphate may well be the basis of the need for an adequate coronary blood supply to sustain what Juvenelle and associates15 term "satisfactory fibrillation," that is, fibrillation that is amenable to countershock defibrillation and survival.

The provision of an adequate coronary blood supply for a fibrillating heart depends in part upon knowledge of the oxygen consumption of the fibrillating heart. Information on this parameter of cardiac metabolism is scant. Hooker and Kehar4 reported an increased carbohydrate metabolism in the fibrillation state based on the perfusion of dog hearts with Locke solution. Such data cannot be adequately compared with our observations concerning the oxidative metabolism of hearts perfused with blood. The experiments reported by Senning3 in which fibrillation did not appreciably alter the myocardial oxygen consumption were well controlled by data obtained during normal sinus rhythm both before and after the fibrillation period. In these experiments, however, the beating left ventricle could do but little external work since the blood flow into the left ventricular cavity was minimal and could only come from the coronary artery drainage into this chamber. The cardiac oxygen consumption as measured by Senning under these experimental conditions would be expected to approximate that existing in the fibrillating heart.

In our experiments the coronary artery–coronary sinus oxygen difference and the myocardial oxygen consumption are significantly lower in the perfused fibrillating heart than in the control state of normal sinus rhythm (table 2). It seems probable that the adequate adenosine triphosphate synthesis observed to occur in the face of this decreased oxidative metabolism in the perfused fibrillating heart can be related to the fact that the cardiac stroke work (stroke volume multiplied by mean systemic blood pressure) is essentially zero in ventricular fibrillation.

**Summary**

The cardiac metabolism of the fibrillating left ventricle of the dog heart with and without the maintenance of left coronary artery blood inflow has been investigated. Measurements of coronary artery blood inflow, coronary artery–coronary sinus oxygen difference, cardiac tissue adenosine triphosphate (ATP), glycogen and in vitro oxygen consumption are presented.

The myocardial adenosine triphosphate and glycogen levels fall progressively after ventricular fibrillation is induced, if left coronary artery inflow is not maintained. The in vitro oxygen consumption of the biopsied tissue is initially elevated. Adequate coronary artery perfusion, however, is able to maintain the ventricular adenosine triphosphate and glycogen content during a 40-minute period of fibrillation, and the in vitro oxygen consumption is unchanged. The reinstallation of left coronary artery perfusion after 30 to 40 minutes of ventricular fibrillation with no coronary blood flow results in the apparent resynthesis of high energy phosphate and the restoration of vigorous, rapid fibrillatory movements.

The coronary artery–coronary sinus oxygen difference and the left ventricular oxygen
consumption are decreased in the perfused fibrillating ventricle as compared with the values of the beating heart. This decreased oxidative metabolism may be related to the fact that the external cardiac work is essentially zero in ventricular fibrillation.

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