Metabolism of the Heart in Failure

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Heart failure may be considered from a variety of viewpoints and studied by diverse methods. Research into the clinical and hemodynamic aspects of congestive failure has uncovered much useful information; however, the basic question remains unanswered: What changes in the myocardium lead to deficient emptying of the heart and thence to heart failure? In recent years, modern techniques have made possible direct study of the cardiac muscle in attempts to understand how it converts energy derived from substrates into useful work and to uncover derangements that may lead to insufficiency and failure of the heart. While this problem is far from solved, progress has been made and unresolved questions have been brought into sharper focus.

Normal Cardiac Metabolism

The heart extracts foodstuffs and oxygen from the coronary blood; energy must be released from the metabolism of foodstuffs and transferred to the effector structures, the contractile proteins of heart muscle. A schematic representation is found in figure 1 in which cardiac metabolism is arbitrarily divided into 3 phases: energy production, energy conservation, and energy utilization. By introduction of a catheter into the coronary sinus, myocardial extraction of substrates and of oxygen may be measured in the intact animal or man without disruption of normal physiology. By determining the content of various foodstuffs or oxygen in simultaneously obtained arterial and coronary sinus blood samples and by measuring coronary flow, the myocardial extraction and usage of these substances may be calculated. It is then possible to obtain the percentage of oxygen utilized in the metabolism of any individual substrate (the oxygen extraction ratio). These studies have shown that the heart can extract glucose, pyruvate, lactate, fatty acids, amino acids, and ketones from the arterial blood. The actual myocardial extraction of carbohydrates varies within certain limits with the arterial concentration. Thus, in the postabsorptive state the oxygen extraction ratio of carbohydrates is high, illustrating that under these conditions these substances furnish the major portion of available energy of the heart; in the fasting state, however, utilization of fatty acids accounts for a major portion of the total usage of myocardial oxygen, with an oxygen extraction ratio of 67 per cent as compared to 35 per cent for carbohydrates (table 1). After ingestion of a fat emulsion the oxygen extraction ratio for total fatty acids rises to 132 per cent, suggesting storage or incomplete metabolism of fats.

Recent studies conducted in this laboratory and elsewhere have further defined the myocardial utilization of fatty acids. Gordon and Cherkes have shown that the nonesterified fatty acid fraction of plasma (NEFA) is the lipid fraction primarily concerned with the transport of fats to tissue. These authors demonstrated that NEFAs were extracted by the heart. However, Fredrickson has shown that a large fraction of the chylomicon tri- glyceride appears to be utilized without first appearing in the plasma NEFA fraction. In this laboratory it has been found that less than half of the fatty acids consumed by the
Figure 1
Schematic representation of myocardial metabolism (modified from Olson).1

myocardium are derived from the NEFA fraction.11 These data strongly suggest direct myocardial utilization of the esterified fraction. As opposed to carbohydrates, the myocardial usage of NEFA is not directly correlated with arterial concentration. During alimentary hyperlipemia, heparin induces a moderate rise in the arterial level of NEFAs, but only an insignificant increase in their myocardial usage11 (fig. 2). On the other hand, myocardial usage of NEFA appears to be related to the nutritional state of the moment. When carbohydrate substrates are available, they appear to be used preferentially, while NEFA usage declines. In the presence of readily available carbohydrates, both the arterial NEFA concentration and the myocardial usage of NEFA drop to low levels.12

At cardiac catheterization, the iodine number of the total fatty acid fraction of arterial and coronary sinus blood has been determined in this laboratory. The iodine numbers of the coronary sinus samples are consistently higher than those of the arterial samples, suggesting that the heart utilizes preferentially saturated fatty acids.11

Under normal conditions, the heart extracts most of the available oxygen from the coronary blood.4 Increased demands for oxygen must therefore be met almost entirely by increased coronary blood flow.13 The dependence upon rapid changes in coronary blood flow is evident when one realizes that the heart must be able to meet sudden demands for increased output without incurring an oxygen debt.

Energy is obtained from the available food-stuffs by stepwise degradation taking place primarily in the tricarboxylic acid cycle. The release of energy is almost entirely aerobic and mediated by the respiratory enzymes.14 The energy produced by substrate oxidation must be harnessed; to accomplish this, the energy release is coupled with the formation of high-energy phosphate bonds.15 The heart contains largely adenosine triphosphate (ATP) and smaller amounts of creatine phosphate, which probably functions as a high-energy phosphate reservoir. On the average, about 3 molecules of high-energy phosphate are produced for each atom of oxygen utilized.16 The energy is then held as high-energy phosphate until employed by the contractile proteins. Since it has been found that the arrested heart requires about 20 to 35 per cent as much oxygen as does the quietly beating heart,17 one may calculate that 65 to 80 per cent of the phosphate energy bond is utilized for muscular contraction. If allowances are made for the energy requirements of the non-beating heart, the left ventricle converts about 38 per cent of the available oxidative energy into useful work.18

Myocardial energy then is made available by substrate oxidation and is captured and conserved as high-energy phosphate, but the burden of the actual work of the heart falls to the contractile proteins, actin and myosin.19

The discovery that the muscle proteins, actin and myosin, combine to form actomyosin complex, the contractile protein in muscle,

<table>
<thead>
<tr>
<th>Carbohydrate, %</th>
<th>Noncarbohydrate, %</th>
</tr>
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<tbody>
<tr>
<td>Glucose 17.90</td>
<td>Fatty acids 67.0</td>
</tr>
<tr>
<td>Pyruvate 0.54</td>
<td>Amino acids 5.6</td>
</tr>
<tr>
<td>Lactate 16.46</td>
<td>Ketones 4.3</td>
</tr>
<tr>
<td><strong>TOTAL</strong> 34.90%</td>
<td><strong>TOTAL</strong> 76.9%</td>
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Table 1
Relative Contribution of Carbohydrates and Non-carbohydrates to Total Myocardial Oxygen Usage in the Postabsorptive State
by proteolytic digestion into 2 components, only one of which is endowed with adenosinetriphosphatase activity. This adenosinetriphosphatase activity plays an important role in muscular contractions by breaking down ATP, a high-energy phosphate compound, into adenosine diphosphate (ADP) and inorganic phosphate, thus making the energy available for muscular contraction. Actin is obtained from the muscle residue from which myosin and all other soluble proteins have been extracted; a globular or G form is contained in aqueous extracts, but salts change this into the fibrous or F actin. Here, too, ATP is important, since it is involved in the polymerization of actin and may be an important part of the actin molecule. One of the most striking properties of F actin is its ability to form a complex with myosin, leading to the formation of actomyosin; this compound has high viscosity and possesses a considerable degree of adenosinetriphosphatase activity in the presence of magnesium. When ATP is added to actomyosin, striking physical changes, such as a drop in viscosity, occur. Although actual mechanisms remain unknown, it is probable that the interactions among actin, myosin, actomyosin, ATP, and the various ions are responsible for the events taking place during contractions of skeletal and heart muscle.

It is of particular interest to those concerned with the molecular basis of heart disease, that these contractile proteins of the heart can be studied in systems that stand halfway between the whole muscle and protein enzyme preparations. There exist several of these models. In one of these, ions including potassium and sodium as well as ATP have been removed by prolonged extraction of the muscle strips in water and glycerol. These glycerinated fiber models contract upon addition of ATP. Another method for reconstruction of a model of the contractile system consists in producing surface films of actomyosin solution that can be compressed into bands. With this method, one can record, without appreciable friction, shortening of the band at considerable magnification.

Figure 2

Top. The effect of heparin on the average arterial plasma concentrations of total fatty acids (total FA) and nonesterified fatty acids (NEFA) in 8 dogs. Bottom. Simultaneous myocardial usage of total FA and NEFA in the same 8 dogs. Despite a rise in the arterial NEFA levels there is only minimal increase in the NEFA utilization.

has shed much light on the nature of the alterations occurring in contracting muscle at the molecular level. The muscle protein myosin itself has ATPase activity, which is inhibited by magnesium and activated by calcium. Actually, myosin itself can be split...
Heart Failure

The dynamic manifestations of cardiac failure from any cause are similar. There are no reasons, however, for assuming that the underlying mechanisms of different types of failure are the same or even similar. For the purpose of this discussion, failure of the heart is divided into 3 groups. Under group I, heart failure associated with prolonged overload of the heart muscle fibers such as occurs with hypertension, valvular heart disease, and arteriosclerotic heart disease is considered. In support of this particular grouping is the fact that the myocardial metabolism of the members of this group appears to be identical. Group II consists of all the types of heart failure in which a metabolic factor may be involved. Each entity in this group is considered separately without the implication that the underlying causes are similar. Lastly, group III consists of the failure of the isolated heart.

Group I

Chronic congestive heart failure such as occurs with hypertension, valvular heart disease, and arteriosclerotic heart disease is difficult to obtain experimentally. As a result, most of the data has been obtained in human beings. Studies have been published on the utilization of myocardial substrate in normal individuals, in patients with compensated heart disease, and in those with congestive failure. Myocardial uptake of glucose, pyruvate, fatty acids, and ketones was not altered by heart disease or by chronic congestive failure (fig. 3). In addition to normal myocardial usage of substrates, patients with compensated or decompensated heart disease have normal coronary blood flow and normal myocardial oxygen usage per weight of heart muscle, despite increased diastolic heart size (fig. 4). Since the failing heart during exercise can increase its oxygen uptake, there appears to be no impediment to the delivery of oxygen to the myocardium.

Digitalis preparations do not affect coronary blood flow or myocardial oxygen consumption significantly in the normal or failing human heart. There is no significant effect of lanatoside-C on utilization of myocardial substrate despite improvement of the work capacity of the failing heart. Thus, myocardial substrate utilization, oxygen consumption, and coronary blood flow are not significantly affected in patients with congestive heart failure included in group I, nor is there any change as the heart failure recedes after digitalis. Essentially similar results have been found by other investigators.

The normal utilization of substrates and oxygen by the failing heart suggests that the underlying defect may be located in energy conservation or utilization. A relative lack of high-energy phosphate due to rapid deterioration or inefficient formation from normal oxidation must still be considered. Wollenberger demonstrated that heart failure could take place in the dog heart-lung preparation in the presence of normal or even elevated levels of high-energy phosphate. This is in line with the report of Olson and Piatnek that levels of ATP and creatine phosphate are also normal in chronic and congestive heart failure in dogs with induced valvular disease.

Figure 3
Relative contribution of the individual foodstuffs to oxidative metabolism of the normal and failing heart. It may be seen that the differences between the 2 groups are minimal. The respiratory quotients are essentially the same. (Republished by permission of the American Journal of Medicine.)
Furthermore, oxidative phosphorylation in mitochondria obtained from heart of guinea pigs in chronic congestive failure is normal. 33

Therefore, by exclusion, the evidence points to the organs of energy utilization, the contractile proteins, as the site of the derangement in the myocardium of this group. Studies undertaken on actomyosin bands, although not yet conclusive, support this contention. Thus, it has been shown that the contractility of these bands from hearts of human subjects dying from congestive failure is impaired. Digoxin failed to correct this defect, but the combination of Digoxin and calcium chloride restored the normal contractility. 22 Benson has demonstrated that both the concentration and the viscosity of actomyosin are reduced in dogs with chronic heart failure secondary to surgically produced valvular disease. 34 Later he and his co-workers found impaired contractility of glycerol extracted muscle bundles from the chronically failing canine heart. 25 Physiochemical characterization of myosin by Olson and co-workers has given considerably higher estimates for molecular weights of myosin prepared from failing than from normal hearts; differences in molecular configuration of myosin were also described. 36, 37

More information is still needed before the basic underlying defect in congestive heart failure is clearly delineated. However, certain tentative conclusions are warranted. For example, it is likely that alterations in the molecular structure of contractile proteins induced by chronic stretch of these fibers may lead to deficient contractility of the heart in congestive failure. In addition, in both heart failure as seen in this group and in failure of the heart in the heart-lung preparation, the myocardial oxygen consumption is normal or diminished. It is apparent from several studies that the oxidative functioning of heart muscle sarcomeres, like liver mitochondria, is under some sort of regulatory system. It has been mentioned in previous paragraphs that during muscle contraction and elongation ADP is formed from ATP. Thus, the main source of ADP in the muscle cell is the actomyosin system itself. 38 In addition, mitochondria are responsible for the formation of ATP. Changes in contractile proteins may result in diminished formation of ADP from ATP because of defective adenosinetriphosphatase activity. Lardy and Wellman have shown that ADP formation must occur in order to achieve oxidation of substrates. 39 Consequently, failure to increase oxygen utilization when the heart is dilated in failure may be related to lack of increased release of ADP by malfunction of contractile proteins. Studies concerned with the adenosinetriphosphatase activity of actomyosin prepared from human hearts would be of great theoretical and practical interest.

Group II
Anoxia and Anoxia

As stated previously, this group includes heart failure in which a metabolic factor may be involved. Increased cardiac output and tachycardia are known to exist in this condition. Because of the decreased blood oxygen carrying capacity the myocardial oxygen ex-

**Figure 4**
Myocardial oxygen consumption. In 22 patients with congestive failure the mean coronary flow was slightly lower than the average found in 16 normal patients. However, the coronary arteriovenous oxygen difference in the decompensated patients was sufficiently increased so that the oxygen consumed by equal weights of heart muscle was the same in both groups. (Reproduced by permission of the American Journal of Medicine. 13)
traction falls. However, the coronary blood flow rises markedly and the total myocardial oxygen consumption may be higher than in the normal person. Experiments in the open-chest dog have shown similar results in coronary blood flow in response to anemia. When the hematocrit is reduced to levels of 24 to 31 per cent, there is depression of ventricular function curve. This loss of the ability of the heart to increase its work occurs when the coronary bed is near maximum dilatation, suggesting that, despite coronary vasodilatation, delivery of oxygen to the myocardium is inadequate. The mechanism of rapid spontaneous failure of the heart in the heart-lung preparation under anoxic conditions is probably comparable to that described in anemia; it is likely that in both conditions failure is the result of inadequate energy production by the heart. Thus, Favaz and associates have shown that under anoxic conditions, the creatine phosphate content of the isolated heart is reduced. Experiments in this laboratory have furthermore demonstrated that during anoxia there is a rapid diminution of creatine phosphate, ATP, and glycogen, while the level of hexosemonophosphate increases. The changes are compatible with rapidly progressing glycolysis, and suggest that under these conditions the enzyme phosphofructokinase may be the rate-limiting enzyme. Even brief anoxia, as present during angina pectoris, and localized anoxia during myocardial infarction lead to demonstrable glycolysis, as evidenced by increased lactate levels in coronary sinus blood.

Myocardial Failure in Hemorrhagic Shock and Myocardial Infarction

Myocardial anoxia is also responsible for myocardial failure observed under these circumstances. In hemorrhagic shock, the myocardial oxygen consumption is diminished during both the oligemic and the normovolemic phase and localized ischemia is present in coronary occlusion. In hemorrhagic shock, observations on the effective atrial pressure, ventricular volume changes, and intraventricular pressures have demonstrated that the deterioration of myocardial expulsive power contributes to progressive circulatory failure. Circulatory failure even persists after restoration of normal blood volume, demonstrating the presence of an irreversible state (the normovolemic phase). The diminution in coronary flow results in definite disturbances in general metabolism, in which the heart is also involved. There is evidence that generalized systemic glycolysis and concentrations of pyruvate in coronary venous blood are increased above those of arterial blood; the myocardial extraction and usage of glucose is also diminished.

Myocardial infarction also leads to acute myocardial failure if the uninvolved portion of the myocardium fails to compensate for the loss of contractile power of the ischemic muscle. Under these circumstances, there is a decrease in stroke volume and a compensatory increase in peripheral resistance. Metabolic changes suggest that myocardial ischemia is accompanied by rapid glycolysis taking place in heart muscle. Pyruvate and lactate concentrations in coronary venous blood frequently exceed those in arterial blood. Myocardial glycolysis is also present in the arrested and fibrillating perfused heart. This disturbance in energy production may conceivably lead to diminished expulsive power of the heart and to progressive circulatory failure.

Hyperthyroidism

Thyrotoxicosis is frequently associated with congestive heart failure but the failure may be reversed following adequate therapy. The increased total-body oxygen consumption, cardiac output, and heart rate are well recognized. However, increased cardiac load seems inadequate to account for the associated heart failure and metabolic factors have often been suggested. Early studies with coronary sinus catheterization suggested that the oxygen consumption of the heart in thyrotoxicosis was normal; however, as more patients were studied, it became apparent that the heart of both thyrotoxic man and dog did partake in the general increase of body metabo-
although recent observations cast doubt on this supposition. The coronary blood flow, the myocardial substrate utilization, and the oxygen consumption are all increased. Myocardial oxygen utilization returns to normal following remission of thyrotoxicosis. Normal myocardial extractions of glucose, lactate, and pyruvate have been reported in thyrotoxic patients; in hyperthyroid dogs these extractions were diminished. Thyroid hormone results in "uncoupling" of oxidative phosphorylation, leading to inefficient energy conservation; under these conditions more oxidation of substrate is required to produce the same amount of high-energy phosphate. Heart mitochondria are particularly susceptible to this effect of the hormone. Therefore, if this effect were present in vivo, one might expect high-energy phosphate compounds to be reduced in the myocardium in the presence of heart failure associated with thyrotoxicosis. Piatnek and Olson could not confirm this in thyrotoxic dogs; however, the animals were apparently not in heart failure and consequently insufficient energy conservation still remains a possible cause of congestive heart failure seen in thyrotoxicosis.

**Thiamine Deficiency**

It is now known that thiamine pyrophosphate (coenzyme for transketolase) catalyzes the reactions of pyruvate to acetyl Co A, and α-ketoglutarate to succinate as well as the transketolase reaction. However, the relationship between these biochemical disturbances and the physiologic manifestations of the disease still remains obscure. The heart muscle like other tissue is unable to utilize lactate and pyruvate normally. In dogs with thiamine deficiency at low rates of coronary blood flow the myocardial oxygen extraction is high; at larger flow the oxygen content of coronary sinus blood is elevated to a greater degree than expected, resulting in a marked diminution of myocardial oxygen extraction. This abnormal relationship between coronary blood flow and myocardial oxygen utilization suggests that deranged metabolism may result in insufficient energy production, which could well account for the decreased ATP levels observed in the hearts of thiamine-deficient rats and may also explain the heart failure seen in beriberi.

**Group III**

*Spontaneous Failure of the Isolated Heart*

Acute myocardial failure can be experimentally produced in the heart-lung preparation; heart failure usually occurs spontaneously 2 to 4 hours after the heart and lungs have been separated from the rest of the organism. Many suggestions have been made to explain this specific failure of the isolated heart, but there have been no definite conclusions. Heart failure in the isolated heart has some mechanical features in common with chronic heart failure as it occurs in patients with congestive heart failure. In both instances there is an increase in the end-diastolic pressure and diminution of the stroke volume. However, there are notable differences. In the first place, the element of hypertrophy is missing. Secondly, the oxygen consumption of the isolated heart is diminished, while that of the failing heart in situ remains normal. Thus, in the acutely failing heart in vitro both cardiac work and oxygen consumption are diminished, while in clinical congestive heart failure the myocardial oxygen consumption remains normal despite the decrease in work.

What is the cause for the spontaneous heart failure occurring in the heart-lung preparation? Several possibilities exist. The first is that it is the result of alterations of the contractile proteins of the heart. Studies have been performed in which the shortening of actomyosin bands prepared from spontaneously failing hearts in the heart-lung preparation were recorded; the contractility of actomyosin prepared from hearts failing in these preparations remained unimpaired. Therefore, it is likely that the mechanism of spontaneous failure does not lie in organs of energy utilization. Since the extraction of substrates by the isolated failing heart remains normal, one must look for disturbances not connected with the utilization of sub-

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strates. A clue to the possible mechanism of spontaneous failure may be sought in the work of Rein, who showed that the inclusion of liver and spleen in the perfusion circuit of a heart-lung preparation increased myocardial efficiency. It is not clear from his studies whether or not the spleen actually releases a substance that is transformed by the liver into the active principle. However, it could be established here, in confirmation of the work of others, that the inclusion of both liver or spleen increases the myocardial efficiency slightly, primarily by a diminution in the oxygen consumption of the heart. Cardiac work is not altered.

The question arose as to the nature of the active principle or principles in these organs. The likelihood existed that spontaneous myocardial failure in the heart-lung preparation results from lack of catecholamines in either heart muscle or the perfusion fluid; the rise in myocardial efficiency resulting from the inclusion of liver and spleen in the perfusion circuit might then be the consequence of partial restoration of the depleted supply of these substances. It is known that the spleen contains large amounts of norepinephrine because of its abundant supply of sympathetic nerve endings. There are also considerable amounts of norepinephrine present in heart, muscle, ciliary bodies, liver, and to a lesser extent, the lung. The concentration of norepinephrine in these organs appears to be related to their adrenergic nerve supply.

In order to prove that lack of norepinephrine is responsible for the spontaneous failure of the isolated heart and that addition of this catecholamine by the spleen or the liver counteracts this condition, it is necessary to answer the questions whether norepinephrine reproduces the effects of liver and spleen on the isolated heart and whether it raises cardiac efficiency by lowering myocardial oxygen consumption without raising cardiac work. In addition, information is essential on the catecholamine content of the spontaneously failing heart or its perfusion fluid. It is known that the infusion of relatively large amounts of catecholamines diminishes the efficiency of the isolated heart, however, the situation is quite different when very small amounts of norepinephrine or dopamine are used in these preparations. This results in an increase in the myocardial efficiency because the oxygen consumption of the heart diminishes while cardiac work is not altered.

Is the heart muscle or the perfusion fluid in the heart-lung preparation depleted of norepinephrine? It has been previously mentioned that the heart contains appreciable quantities of norepinephrine. Experiments were performed in which the norepinephrine content of hearts rapidly removed from the animal was compared to that of the heart maintained in the heart-lung preparation for at least 1 hour. There is no appreciable difference between the 2 preparations. This finding illustrates that the presence of nor-

Figure 5

Catecholamine content of the dog heart. Twenty minutes after addition of dihydroxyphenylalanine (Dopa) to the heart-lung preparation, the catecholamine content is normal. At this time the efficiency of the heart had been improved. Two hours later the heart was failing despite high myocardial concentration of catecholamines.
Studies on the catecholamine content of the perfusion fluid of the heart-lung preparation suggest a significant diminution of these substances (fig. 6). This information is based on the determination of catecholamines with the potassium ferricyanide method of Euler which determines only compounds carrying the amide group, on which pharmacologic activity depends. It is also possible that lack of cholinergic substances is a contributing factor.

**Conclusion**

Investigations of the 3 phases of cardiac metabolism—energy production, energy conservation and energy utilization—have shown marked differences in the underlying mechanisms of heart failure. Thus, in failure with prolonged overload of the myocardium as occurs with hypertension, valvular heart disease, and arteriosclerotic heart disease (group I), an abnormality of energy utilization seems most likely. In the diverse situations with heart failure considered under group II, there appears to be a defect in energy production or conservation. In anemia, myocardial failure results in insufficient transport of oxygen for substrate metabolism, while in hyperthyroidism uncoupling of oxidative phosphorylation may lead to failure of energy conservation. In beriberi heart disease a deficiency of thiamine pyrophosphate (coenzyme) produces a breakdown of certain specific decarboxylation reactions that appear to interfere with normal myocardial energy production. In hemorrhagic shock and myocardial infarction, general or localized anoxia leads to defective energy production.

Spontaneous failure occurring in the heart-lung preparation is in all likelihood the result of diminished catecholamine and cholinergic substances of the perfusion fluid.

It is apparent from this review that no common denominator exists as a cause of heart failure. Rather at the base of the uniform dynamic manifestations of this condition are multifarious disturbances in energy production, conservation, and utilization.
Conclusion in Interlingua

Investigationes del 3 phases del metabolismo cardi-a—production de energia, conservasion de energia, e utilisation de energia—ha revelate marcate diferentias in le subjacente mechanismo del disfallimento cardio. Assi, in disfallimento con long duration super-cargamento del myocardo—como illo occurre in hypertension, morbo de valvula cardia e morbo arteriosclerotic del corde (hic designate como morbos de grupo I)—le presentia de un abnormalite in le utilisation de energia es molto probable. In le diverse situationes associate con disfallimento cardio le quales es hic considerate sub gruppo II, il pare occurrer un defecto in le conservasion o in le production de energia. In anemia, disfallimento myocardial resulta in un insufficiente transporto de oxygeno pro le metabolismo del substrato, durante que in hyperthyroidismo le discopulation de phosphorylation oxydator pot resultant in un disfallimento del conservasion de energia. In morbo cardi beriberi, un deficientia de pyrophosphato de thiamina (ecocarboxylase) produce un collapse de cete specific reacionates de discarboxylation e isto par disturbar le normal production myocardial de energia. In choc hemorrhagie e in infarimento myocardial, anoxia general o localisate resulta in un production defective de energia.

Le disfallimento spontane que occurre in le preparato de corde e pulmon es probabilissime le resultato de un reduce contegoto de catecholamina in le liquido perfusional.

Iste revista rende apparente que nulle denominator commun existe in le causas de disfallimento cardi-a. Al contrario, al base del uniforme manifestationes dynamic del iste condition il ha multiple disturbanzas in le production, le conservasion, e le utilisation de energia.

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