Intracellular Respiration of Myocardium

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The term, respiration, means not only gaseous exchange between oxygen and carbon dioxide in the lung but also oxidation of substrates in the tissue cells. To state the respiration at the intracellular level, it may be important to discuss the mode of oxygen supply to the cell, intracellular diffusion of oxygen through the cellular membrane and utilization of oxygen and oxidizable substrates in cells. In this symposium the mechanism of intracellular respiration, especially in myocardial cells, and speculation on some metabolic regulations in the cellular respiration are presented.

There are three factors to be considered on the intracellular respiration. They are (1) intracellular exchange oxygen and carbon dioxide, (2) mobilization and utilization of oxidizable substrates and (3) mode of terminal oxidation coupling with phosphorylation.

The first problem, intracellular gaseous exchange, has been clarified physiologically as same as the mechanism of alveolar gaseous exchange in the lung. This problem will not be expatiated more.

Secondly, the problem of mobilization and utilization of substrates is the matter in question. It is well known that glycogen, glucose, pyruvate, lactate, non-esterified fatty acid (NEFA), ketone bodies and amino acid are utilized in myocardial cells. Among these substrates, glucose and its intermediates (pyruvate, lactate and so on) and NEFA are most important as energy sources. Glucose and its intermediates are derived from the alimentary tract via the liver. NEFA is mobilized from the adipose tissues through or not through the liver (Fig. 1 & 2).

The problem to be clarified is: which is preferentially utilized, glucose or NEFA? Although this question comprises intricate speculations, it is considered that glucose (blood sugar) is the rather common energy source. When carbohydrate metabolism is impaired in some states such as starvation or diabetes mellitus, NEFA and acetocetate are mobilized briskly from the adipose tissue. Endocrine system and autonomous nervous system regulate these mobilization and utilization. The modes of substrate utilization are somewhat different according to the kind of tissues. In skeletal muscle which is rich in glycogen, energy is well produced in anaerobic glycolysis. One reason may lie in the property of the skeletal muscle tissue that has rather long re-

Fig. 1. Oxygen and substrate supply to heart.

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The third problem of intracellular respiration is the mode of terminal oxidation and oxidative phosphorylation. The site of oxidation of the substrates is well known as the tricarboxylic acid cycle (TCA cycle). However, oxygen molecule does not directly combine with substrate molecule in TCA cycle. First, substrates are dehydrogenated and the hydrogen ion is carried in the electron transfer chain. Finally, reduced cytochrome A is combined with oxygen molecule which is carried by hemoglobin. At two to three sites of the electron transfer chain, ATP synthetizing systems are coupled (Fig. 3).

It has been considered that the intracellular respiration may be regulated in some way at this level. With the advancement of the study on mitochondrion, in which the terminal oxidation coupled with phosphorylation is arranged, the regulation mechanism of intracellular respiration has also been elucidated. Chance and his coworkers showed polarographically three factors regulating the mitochondrial respiration. They are oxygen, substrates and phosphate acceptors (ADP, predominantly). Mitochondrial oxygen consumption rate increases when these three factors are complete (state 3). When ADP is absent, the rate is very slow even though oxygen and substrate are both present sufficiently (state 4) (Table 1). Therefore, there is a regulation mechanism of cellular oxygen consumption by ADP. This mechanism is termed as respiratory control by Chance et al. As ADP is produced excessively after muscular contraction, the activity of intracellular respiration in possibly enhanced by
of energy utilization, is regulated viceversa by objected energy utilization, i.e. muscular contraction.

As above-mentioned, intracellular respiration finally means oxidative phosphorylation. It is noteworthy that oxidative phosphorylation is involved in some pathologic states of the tissues. Details of this phenomenon have been described elsewhere. Although oxygen supply is sufficient and substrates are oxidized adequately, intracellular respiration should not be denoted normal when ATP synthesis is disordered. Furthermore, if respiratory control is deteriorated, intracellular respiration should be regarded as abnormal though ATP synthesis is carried out somehow (Fig. 4). In this point of view, intracellular respiration should not be discussed merely with the data of gaseous exchange and/or utilization of substrates. It is the time for the intracellular respiration to be researched more prudently on the intracellular regulation systems.

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Table I  Factor Regulating Mitochondrial Oxygen Consumption

<table>
<thead>
<tr>
<th>Oxygen</th>
<th>+</th>
<th>-</th>
<th>+ or -</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substrate</td>
<td>+</td>
<td>-</td>
<td>+ or -</td>
</tr>
<tr>
<td>Phosphate Acceptor (ADP)</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Oxygen Consumption Rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State (CHANCE)</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

+ : present  - : absent

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Fig. 4. Pylosophy on respiration.