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The Relationship between Mitochondrial Structural Changes and Respiration Rate in Intact Mucosal Cells

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We have shown in our earlier work that slices of rat jejunal mucosa will respire at a high rate when they are incubated with an amino acid mixture (Jasper & Bronk, 1968). Electron micrographs of mucosal tissue show that under these conditions a high proportion of the mitochondria become condensed. This change in structure involves a shift in volume from the inner compartment to the outer compartment and a close association of dense matrix material with the inner membrane. Although these mitochondrial structural changes are associated with high rates of mucosal respiration they do not occur in the presence of the uncoupler 2,4-dinitrophenol.

Recently we have been investigating in more detail the extent to which these mitochondrial structural changes are linked to a rapid rate of mucosal respiration. Several lines of evidence have made it questionable that mitochondrial condensation is obligatory for oxidative phosphorylation. Thus the presence of glucose in the incubation medium is more effective in preventing the changes in mitochondrial structure than in decreasing cell respiration. Also, when mucosal tissue was obtained from animals in different thyroid states, the same type of condensation was observed over a wide range of respiratory rates.

Even more important evidence was obtained by following the time-course of the development of mitochondrial condensation. Polarographic recordings showed that the maximum respiration rate was reached after 15–20 s of incubation. Also, electron micrographs revealed that the characteristic changes in mucosal cytoplasm that accompanied incubation in the amino acid mixture were well advanced after an incubation period of 30 s. By contrast the mitochondrial structure was not condensed after 30 s, and only after an incubation period of about 3 min could the fully condensed structure be observed. In our view these results indicate that the development of the condensed mitochondrial structure lags behind the

initiation of a rapid rate of electron transport. This contrasts with the view expressed by Harris, Penniston, Asai & Green (1968) and others that mitochondrial structural changes are required for the process of energy conservation. From our observations it would appear that, although these changes are a consequence of a high rate of coupled oxidative phosphorylation, they are not essential for the process.

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Factors Affecting the Production of Ketone Bodies during Fatty Acid Oxidation by Isolated Rat Liver Mitochondria

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Isolated mammalian liver mitochondria, unlike those of heart and muscle, can oxidize added fatty acids by two pathways. One pathway leads to the complete oxidation of the fatty acids to carbon dioxide and water. The end products of the other pathway are the ketone bodies. The initial formation of acetyl-CoA during β -oxidation is common to both pathways.

A study has been made of the factors that may determine the distribution of acetyl-CoA between the two pathways during fatty acid oxidation by isolated rat liver mitochondria. No intermediates of the tricarboxylic acid cycle were added to the reaction medium. Oxygen uptake was measured manometrically. The production of ketone bodies was measured by determining the amounts of acetoacetate and β -hydroxybutyrate in the deproteinized reaction medium by the enzymic method of Williamson, Mellanby & Krebs (1962). If it is assumed that no intermediates accumulate, the relative contribution of the two pathways can be calculated from these results.

It was found that two factors, which had hitherto not been recognized, may in certain conditions greatly influence the relative importance of the two pathways of fatty acid breakdown. These factors are the concentration of inorganic phosphate and the presence of bovine serum albumin.

When 1 mM-DL-palmitoylcarnitine was oxidized in the presence of 0.1 mM-2,4-dinitrophenol and in the absence of added inorganic phosphate, 24% of the

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