OXIDATIVE PHOSPHORYLATION IN MITOCHONDRIA OF THE RAT LIVER AT DIFFERENT STAGES OF REGENERATION

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Absorption of O_2 and oxidative phosphorylation in the mitochondria of rat liver were studied at various periods of regeneration: 12 h, and 1, 1.5, 2, 3, 6, and 12 days after partial hepatectomy. The coefficient of oxidative phosphorylation remained practically constant throughout the period of investigation.

It is therefore postulated that the regenerating and intact livers are chemically indistinguishable, and the formation of much of the energy in the regenerating liver takes place by the same mechanisms as in the normal liver.

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Biochemical data on liver regeneration are extremely contradictory in many respects. Some investigations [3, 13-15, 17] have revealed no essential biochemical changes in the regenerating liver. Other reports, however, describe inhibition of succinate dehydrogenase [2], malate dehydrogenase, oxaloacetate oxidase, cytochrome oxidase [15], and glutamate dehydrogenase [10] during regeneration, which cannot be harmonized with data showing an increased O_2 consumption by regenerating liver [1, 7, 16]. The maximal O_2 consumption observed by Perkinson and Irving [16] between the 7th and 14th days of regeneration of the liver is not in agreement with results obtained by other workers [9, 12, 18, 19] showing that mitotic activity and proliferation of the liver parenchyma reach a maximum in the 2nd-3rd days after the operation.

For the reasons given above it was decided to study the O_2 consumption and oxidative phosphorylation of the mitochondria of the regenerating liver at various times after operation.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats (50 males and 10 females) weighing 150-230 g. The animals were kept on an artificial diet based on the Osborne-Mendel salt mixture as modified by Wesson [20], starting from the 4th-5th day before the operation and continuing until the end of the experiments.

Partial hepatectomy consisted of removal of the left and medial lobes of the liver by the method of Higgins and Anderson as modifed by Crandall and Drabkin [8]. All the rats were fasted for 24 h before the operation and before decapitation. The animals were sacrificed 12 h and 1, 1.5, 2, 3, 6, and 12 days after the operation and mitochondria were obtained from the liver by differential centrifugation.

Oxygen consumption by the mitochondria was determined manometrically in a Warburg apparatus at 26°. The incubation mixture contained the following components (per ml): 45 μmoles K_2HPO_4, 15 μmoles $MgSO_4$, 5.4 μmoles ATP, 4.5 μmoles glucose, 2.5 μmoles α-ketoglutaric acid, mitochondria expressed as protein from 2 to 8 mg, and up to 0.5 mg crystalline hexokinase. Phosphorus was determined by the method of Ferdman and Sopin [6], and protein by Lowry's method.

EXPERIMENTAL RESULTS

The results are given in Table 1. At first glance the course of the changes shown in these results agrees with observations of other investigators [1, 2, 7, 16]. The changes observed are within the limits of experimental error, and are not statistically significant.

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TABLE 1. Oxidative Phosphorylation and O_2 Consumption by Rat Liver Mitochondria at Various Stages of Regeneration

Days after operation	O_2 (in μatoms/h/mg protein)	P/O
0	2,44±0,45 (8)	2,80±0,11 (6)
0,5	2,56±0,26 (7)	2,62±0,30 (6)
1	2,50±0,35 (8)	2,53±0,24 (7)
1,5	3,33±0,45 (6)	2,56±0,35 (6)
2	2,96±0,43 (11)	2,77±0,33 (7)
3	2,12±0,67 (6)	2,24±0,49 (5)
6	3,25±0,39 (7)	2,23±0,21 (7)
12	2,51±0,38 (7)	2,45±0,22 (6)

Note. Number of rats given in parentheses.

Since regenerating hepatocytes, as previously established [4], readily undergo fatty infiltration and develop intracellular vacuoles, it is possible that the decrease in the P/O ratio in regenerating liver homogenates observed by Clerici and co-workers [7] is due to the fatty infiltration mentioned above.

The results obtained more probably indicate that no significant changes in oxidative phosphorylation take place in the regenerating liver. This agrees with the findings of Novikoff and Potter [15], who observed no significant changes in the content of lactic acid, ATP, ADP, AMP, and free pentose phosphates, i.e., substrates playing an important role in the accumulation of energy by the liver, and also with results obtained by the study of certain substrates of the tricarboxylic acid cycle [3].

It can thus be concluded that the regenerating liver is indistinguishable from the intact organ in many respects, and most of its energy is formed by essentially the same mechanisms as in the normal liver.

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