

THE EFFECT OF FATTY ACID OXIDATION ON  
GLUCONEOGENESIS IN ISOLATED SHEEP-LIVER CELLS

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Long-chain fatty acids stimulate gluconeogenesis in rat liver (Williamson 1967). We have studied the interaction between fatty acid oxidation and gluconeogenesis in isolated sheep-liver cells.

Parenchymal cells were prepared from the caudate lobe of fed sheep liver by the method of Donaldson et al. (1979), except that 2 mM EDTA rather than EGTA was used. The cells (approximately 5 mg dry wt) were incubated for 60 min at 37°C in 2 ml of Krebs-Henseleit buffer containing 2% defatted bovine serum albumin (Lomax et al. 1979). Rates of gluconeogenesis from pyruvate (2, 5, 10 mM) were determined in the presence and absence of 1 mM palmitate. Oxidation rates of 2, 5 and 10 mM pyruvate [ $1-^{14}\text{C}$ ] and 1 mM palmitate [ $1-^{14}\text{C}$ ] in the presence and absence of each other unlabelled were also measured.

Substrate		Production of		Oxidation of	
Pyruvate mM	Palmitate mM	Glucose nmol/mg	Lactate dw/h	Pyruvate nmol/mg	Palmitate dw/h
2	-	116(20) <sup>b</sup>	133(9) <sup>b</sup>	164(9) <sup>b</sup>	
2	1.0	116(32) <sup>b</sup>	218(3) <sup>c</sup>	126(11) <sup>a</sup>	1.9(0.8) <sup>a</sup>
5	-	111(13) <sup>b</sup>	135(10) <sup>b</sup>	306(30) <sup>c</sup>	
5	1.0	166(12) <sup>c</sup>	310(12) <sup>d</sup>	296(1) <sup>c</sup>	3.4(0.5) <sup>b</sup>
10	-	126(10) <sup>b</sup>	138(8) <sup>b</sup>	519(42) <sup>d</sup>	
10	1.0	294(23) <sup>d</sup>	425(20) <sup>e</sup>	471(41) <sup>a</sup>	3.9(0.7) <sup>b</sup>
-	1.0	18(9) <sup>a</sup>	48(7) <sup>a</sup>		1.7(0.3) <sup>a</sup>

Each value ( $\pm$  SE) is the mean of four sheep, except that only three sheep were used in the pyruvate oxidation experiments. Values with dissimilar superscripts differ significantly ( $P < 0.05$ ).

Rates of gluconeogenesis from pyruvate were maximal at 2 mM but palmitate significantly increased the synthesis of glucose from 5 and 10 mM pyruvate. The rate of synthesis of lactate from pyruvate did not vary with pyruvate concentration but was significantly increased at each pyruvate concentration by the addition of 1 mM palmitate. The oxidation of pyruvate was unaffected by 1 mM palmitate except when at 2 mM. The oxidation of palmitate was significantly increased in the presence of 5 and 10 mM pyruvate.

The increased gluconeogenic rate in the presence of palmitate and the increased rate of  $\beta$ -oxidation is consistent with an inhibition of pyruvate dehydrogenase by acetyl CoA. The increased production of lactate in the presence of palmitate reflects the production of reducing power in excess of the cells' requirements but the significance of this is not obvious.

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