A preceding paper described the "glucose-fatty acid cycle" and included the concept that the oxidation of lipid fuels inhibits the degradation of glucose in muscles. This paper describes investigations of normal subjects on a low-carbohydrate diet and of non-insulin-dependent diabetics, the results of which were compatible with such a mechanism operating in these two situations in vivo. A new possibility was suggested that the primary event in the development of diabetes could be excessive release of fatty acids in adipose tissue and muscle. [The SCI indicates that this paper has been cited over 250 times since 1963.]

C. Nicholas Hales
Department of Clinical Biochemistry
Addenbrooke's Hospital
University of Cambridge
Cambridge CB2 2QR
England

February 1, 1985

This is the third of three papers that I coauthored while a graduate student in the Department of Biochemistry at Cambridge. Surprisingly, all three have been featured in the Citation Classics series. The present paper together with the one on insulin radioimmunoassay represents the work I carried out for my Ph.D. as a graduate student working under the supervision of Philip Randle. I was very fortunate to be a member of Randle's research group at a particularly exciting time. Hal Coore and Randle also devised the simple system that opened up the study of insulin secretion. I should point out, as there seems to be a danger of its being overlooked in these pages, that they showed for the first time that epinephrine inhibition of glucose-stimulated insulin secretion.

The present paper's frequent citation is probably due to its being the early in vivo evidence for the glucose-fatty acid cycle. The cycle seems likely to be important in some states of diabetes. I followed three main themes from this work. The first, in


19