

Summary of Discussion

Dr. Ira G. Wool pointed out that anabolic effects of insulin on liver cells may be independent of adenylyl cyclase. Although liver cells in tissue culture have little if any adenylyl cyclase activity, they exhibit a marked anabolic response to insulin. *Dr. Maurice E. Krabl* suggested that the effect of insulin in the liver may be on the reading of messenger-RNA and cited some experiments by *Tompkins* in support of this hypothesis. It has been observed that insulin will specifically stimulate the formation of tyrosine transaminase in certain hepatoma cells in tissue culture. This effect is not blocked by actinomycin D. This observation has been interpreted as an effect on translation, but in fact it might also be interpreted as an effect of insulin on any event between the formation of messenger-RNA and the synthesis of the enzyme.

Dr. John N. Fain noted that under certain circumstances both insulin and cyclic AMP have the same effect on protein synthesis in liver. Increased protein synthesis initiated by the glucocorticoids appears to be a

transcription effect, while both insulin and cyclic AMP increase protein synthesis through some translational mechanism. *Dr. Fain* further noted that, using a preparation of isolated liver cells, he has been able to confirm all of the effects of insulin and lipolytic agents reported by *Dr. Park*.

Dr. Rachmiel Levine commented that in the depancreatized animal the stimulus effect of glucagon on cyclic AMP would be removed. He wondered if effects of insulin on glycogenolysis and gluconeogenesis can be observed. In response to a question from *Dr. Otto Wieland*, *Dr. Charles S. Park* observed that glucagon will produce a measurable increase in blood and urine cyclic AMP, that this has been observed in both animals and humans, and that presumably the cyclic AMP is released from the liver. This raises the question as to whether cyclic AMP can be a hormone as well as a second messenger. The mechanism by which insulin lowers cyclic AMP levels is as yet unknown.

—JAMES ASHMORE, Ph.D.